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A Record of the Progress of Pharmacy and the Allied Sciences

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THE AMERICAN
JOURNAL OF PHARMACY

VOL. 98 APRIL, 1926 No. 4

EDITORIAL

IN CONVENTION ASSEMBLED

SESQUI-CENTENNIAL year in Philadelphia will witness the gathering of the drug cohorts of America—for the first time in many years—*almost* together. *Almost* together—and that is just where the rub comes.

The American Pharmaceutical Association and its associated organizations meet at the Bellevue-Stratford Hotel—famous for its convention facilities—on August 13th, and the sister organization, the National Association of Retail Druggists, at the same headquarters one week later.

This will be about as near together as the associations have ever met—and it is regrettable that some master amalgamator had not come to bring them into still closer harmony.

There are some who hold that it is not possible nor practical to fuse these groups into one great co-ordinated whole—yet it is only the commonest kind of common sense that sees the advantages to be gained by such a happy fusion.

It is not silly sensationalists—nor idle idealists who have been preaching in convention assembled the good which would come from the All-Pharmacy Amalgamation.

No indeed—rather it is men who have witnessed the gain that came to medicine—the power that came to medicine—the serviceability that came to medicine—when the germ of organization infected that branch of human service.

It is not idle prattle to preach that a kindred good can come to pharmacy when it wakes up to its sense of insecurity—the insecurity that comes from segregated forces—the insecurity that comes from selfish isolation—the insecurity that comes from divided efforts with its multiplied difficulties and subtracted results and added weaknesses.

When it wakes up to its sense of insecurity and realizes that it becomes a worth-while force only when the weight of organization

is back of it—that is when pharmacy *begins* to be a real factor in public service.

If, on the other hand, it is to be content to be a grand old edifice, tumbling—a portion falling into the hands of the chemist—a portion to the hands of the doctor and part to the drugless drug store—then it will not have long to wait if it continues its division of forces. And its forces *are* divided so long as it persists in its present policies.

The commercial interests—represented by retailers and jobbers and wholesalers and manufacturers—in their own groups and conventions, almost ignore the professional group—unmindful of the fact that it is their professional contacts, which give them their class distinction—else they are no different from grocery and drapery and cutlery and other businesses. The professional groups—laboratory workers, teachers, hospital pharmacists and others—seem willing enough to co-operate—although they appear pained and awkward about removing their high hats.

Yet preaching and writing editorials will not do much toward effecting this consolidation. But the Philadelphia idea may well be duplicated at another time—*only* let the associations meet conjointly, in time and place—and so effect a happy economy of entertainment, of time and money—and a solidarity of force and fact that the new pharmacy may become a potential factor in guiding its own destinies to such a state that it will attain to its proper rank in public service and in public opinion.

Let it be hoped that the meetings in Philadelphia will tend us all towards this notion of the All-Pharmacy Amalgamation.

IVOR GRIFFITH.

SELECTED EDITORIAL

INTERNATIONAL UNIFORMITY

THE first step towards unification of standards in medicine was taken in 1864—sixty-two years ago—when the three pharmacopœias of London, Edinburgh, and Dublin became merged in the British Pharmacopœia. Since then a constantly increasing tendency towards international uniformity has been evident. At the second International Conference for the Biological Standardization of Medicaments, recently convened by the Health Committee of the League of Nations, certain proposals were adopted regarding such substances as arsenobenzol, digitalis, ergot, insulin, pituitary, and thyroid. In

these days of travel and intercommunication between countries some uniformity in the matter of potent medicinal substances is a necessity, and there is little doubt that in a short time such uniformity will obtain throughout the civilized world. While an International Pharmacopœia is yet a dream, it is quite possible that in few years an international volume containing standards for potent medicaments may be in circulation.

Meanwhile there are other lines in which also uniformity is desirable. One of these is nomenclature. The names by which a new drug is known are frequently a source of confusion to all concerned. Such products are usually known at first under their proprietary names. When they have obtained full recognition as therapeutic agents they are adopted by an unofficial formulary, such as the British Pharmaceutical Codex, by another name, and later by the Pharmacopœia itself under a third name. Meanwhile in practice the drug is usually still called by its original appellation. A case in point is that of salvarsan; originally known as "606," registered as "salvarsan," adopted by the B. P. C. as "arsenobenzol," and by the U. S. P. as "arsphenamine," this substance is still referred to by many under its original name or number. In the matter of nomenclature the United States Pharmacopœia has set a good example, inasmuch as their names are as a rule well chosen, but it is unfortunate that in choosing names the compilers should have ignored those already in use in this country. Adrenalin they style epinephrine; ethocaine is known as procaine; hexamine has now become methenamine. Such differences cause confusion in medical literature; they tend to prevent the adoption of the new name and cause prescribers and authors to fall back on the original and better known trade-name. Some effort at international uniformity in nomenclature is most desirable.

One other matter may be touched on while this subject is discussed—the universal adoption of the metric system. The Pharmacopœias of both Britain and America have introduced this system throughout, and it remains for the medical profession to adopt it in practice. The system is simplicity itself, as compared with the old apothecaries' weights, and only a very little practice is necessary to enable a prescriber to use it always. We have consistently advocated its use in prescribing for a number of years, and signs are not wanting that our efforts, and those of others working on the same lines, are bearing fruit. Such reforms are bound to come slowly, but come they will, and the sooner the better for all concerned.

ORIGINAL ARTICLES

I. SOME STUDIES ON THE SO-CALLED "WESTERN" (South Dakota) OIL OF AMERICAN WORMSEED

II. DISTILLATION REPORT FOR 1924

III. THE ORIGIN, NATURE AND PHYSIOLOGICAL ROLE OF THE ESSENTIAL OIL

Anton Hogstad, Jr.*

Introduction

THE RESULTS as embodied in the 1923 distillation report seemed to fully justify a continuance of this work, especially in relation to the factor of seasonal variation, the latter no doubt playing a very important role in connection with the elaboration of drug plant constituents.

The scope of the work for 1924 was materially enlarged upon over that of 1923. Approximately two acres of herb were placed under cultivation. In order to properly handle this amount of herb, the Division of Pharmacy purchased a boiler plate steel still capable of receiving a charge of herb ranging from 300 to 500 pounds, depending upon the nature of the herb.

In view of the fact that the 1923 distillations were conducted entirely upon fresh herb instead of air-dried herb, it was deemed advisable to keep this factor constant throughout the 1924 season, although it had been previously recognized that air-drying of the herb no doubt produced a beneficial effect on the nature of the essential oil in relation to the percentage yield of ascaridol. However, the wormseed problem is one that entails considerably more than merely attempting to secure an oil with a high percentage of ascaridol, for in fact it would appear that a high percentage of ascaridol is a detrimental factor rather than one to be desired, as will be discussed in another section of this paper.

The 1924 distillations were conducted in a similar progressive manner to that of 1923, beginning before the period of flower for-

*Professor Hogstad has recently severed his connections with the South Dakota State College Division of Pharmacy, and is at present continuing his advanced studies for the Ph. D. degree in the Biochemical Division, University of Minnesota, Farm Campus, St. Paul, Minnesota.—(*Editor.*)

mation and continuing at regular weekly intervals or thereabouts, for the remainder of the season. Owing to an unavoidable delay in the shipment of the new steel still, the first four batches of the 1924 herb were subjected to steam distillation in the autoclave type of still as utilized for the 1923 distillations.

The paper dealing with the "Origin, Nature and Physiological Role of the Essential Oil" was started in the spring of 1923. The object of this investigation was that of a parallel study to the work dealing with the mechanical steam distillations, in order to seek a solution, if possible, to some of the many difficulties encountered in the semi-commercial production of the essential oil and also to note the various steps in the elaboration of the essential oil within the living plant.

Owing to the complexity and elusiveness of this latter investigation involving a study of the secretion of an essential oil within the living plant, the investigation was continued throughout the 1924 season, in order to substantiate or revise the findings of 1923, and also to obtain additional photomicrographs so as to have a more representative collection from which to choose for publication purposes.

II. DISTILLATION REPORT FOR 1924

Cultivation and Preparation of Herb

Many attempts have been made at the South Dakota State College to sow the seed in a broadcast fashion in specially prepared beds both during the spring and fall, but without much success. Therefore it has been necessary to resort to greenhouse facilities for the production of the thousands of seedlings in the work of the past five years. The seeds were sown in regulation size seed pans, very little difficulty encountered in the securing of a sufficient number of seedlings. The seedlings were later transplanted to other pans, approximately 100 seedlings per pan. Before transferring to the open field, the seedlings were placed in cold frames for a period of about two weeks. No difficulty was experienced in the transplanting of the seedlings to the open fields. They were set at a distance of three feet from each other in the rows, the rows being four feet apart. Transplanting to the open field, as a rule took place during the first week in June.

In the preparation of the herb for distillation, it was cut during the afternoon previous to the day of distillation, trimmed by means of large knives, the lower basal woody portions being rejected. The

trimmed herb was then weighed and loaded directly into the still, and everything put in readiness for the steam distillation on the following morning.

Description of Distillation Unit

The new boiler plate steel still measured three by five feet (tank measurements), being mounted upon legs three feet in length. The tank was constructed of one-quarter inch boiler plate steel and was

Distillation unit as utilized for the production of the 1924 oils. A batch of fresh trimmed herb may be noted on the platform with rejected basal woody portions below.

provided with a removable dome-shaped cover, the latter being fastened by means of some fifty swing bolts. The bottom of the tank was rounded to allow for ample drainage. An outlet valve was inserted in the center of the bottom, and was connected in such a manner with the steam inlet pipe, so as to allow for a complete discharge of the condensed steam in the pipes leading from the boilers of the college heating plant to that of the still. By such an arrangement it was possible to completely discharge all of the condensed steam before allowing the live steam to enter the distillation chamber. The steam inlet entered the tank approximately four inches from the

bottom being attached to a T-shaped distributor pipe within the chamber. Numerous holes, one-eighth of an inch in diameter were drilled through the upper side of the steam distributor pipe, so as to allow for a rapid distribution of the live steam.

A heavy wire screen floor rested upon four metal projections, the screen being approximately eight inches above the bottom of the tank. The still was provided with safety valve, steam gauge, all of which along with the control valve to the inlet pipe were placed at convenient points on the tank above the wooden platform that surrounded the still.

The condenser was the same as utilized for the work of the 1923 distillations, with but one change in its construction. In place of the four single lengths of seven-eighth inch piping, the condenser pipes were arranged so as to allow for two sets of three pipes each, thus making the vapors traverse the length of the twelve-foot condenser box three times as compared to once as in the case of the 1923 distillations.

General Method of Distillation

The time required for a single distillation ranged from fifteen to thirty minutes, the average run being from fifteen to twenty minutes. The steam pressure at the boilers of the college heating plant ranged from 80 to 100 pounds, the pressure allowed at the still was from fifteen to thirty pounds. It required as a general rule, from eight to ten minutes for the first signs of the distillate to appear after the live steam had been turned into the distillation chamber.

The distillate was collected in two one-gallon bottles, the time required to fill the bottles being about four minutes. The temperatures of the distillates were recorded as per Table II. The oil was separated by a series of one-gallon funnels provided with cork stoppers attached to one-eighth inch wooden rods. The one-gallon lots of distillate were allowed to remain in the funnels until there was a sharp division line between the two distillates.

If the amount of oil from the two one-gallon lots of distillate was of a sufficient quantity so as to allow for the physical constant determinations, the oils thus secured were placed in separate bottles. By the adoption of this procedure, it has been possible to secure data relative to the physical constants of the various fractions. The oils were again separated by means of separatory funnels and then filtered.

TABLE II

Lab. No.	Date of Cutting	Date Distilled	Character of Herb	Net Weight Pounds	Time Distillation, Min.	Pressure	Temp. Distillate	Distillate Gallons	Amt. Oil cc. Filtered	S. G. 25° C.	Ascaridol Per Cent.	Refractive Index 20° C.	Optical Rotation 25° C. 100 mm. tube	Solubility 70 Per cent. C_2H_5OH
1	July 21	July 22	Non-flowering—140 plants	101	37	10–15	50–60	14	trace	.....	..	.....	.....	.....
2	Aug. 4	Aug. 5	Chiefly non-flowering—150 plants	140	30	10–15	50–60	14	12	.....	2–3	.....	.....	.....
3	Aug. 5	Aug. 6	Same as No. 2—150 plants	185	25	10–15	50–60	12	20	.....	4	1.4745	.....	Insol. 1:8–1:15
4	Aug. 6	Aug. 7	Earliest stage of flowering	110	21	10–15	50–60	10	3	.....	..	1.4848	.....	Insol. 1:8–1:15
5	Aug. 19	Aug. 20	Earliest stage of flowering	250	27	15	60–65	18	80	0.8431	6	1.4750	—19.421°	Insol. 1:8–1:15
6A					28	12–15	50–60	16	409	0.8495	4	1.4745	—12.423°	Insol. 1:8–1:15
B	Aug. 28	Aug. 29	Chiefly unexp'd flowers h'ds	180	27	12–15	50–60	12	25	.....	..	.....	.....	Insol. 1:8–1:15
7A					15	15–25	50–60	12	1016	0.8552	12	1.4760	—11.548°	Insol. 1:8–1.15
B	Sept. 4	Sept. 4	Partially mature herb	412	26	25	50–60	18	70	0.8436	2	1.4761	—11.853°	Insol. 1:8–1:15
8A					20	25	45–55	12	800	0.8577	10	1.4760	—14.522°	Insol. 1:8–1:15
B	Sept. 11	Sept. 12	Less mature than No. 7	372	30	25	45–55	16	40	0.8778	..	1.4795	—12.888°	Insol. 1:8–1:15
9A					4	20–25	25	2	170	0.8974	26	1.4750	—15.124°	Insol. 1:8–1:15
B					4	25	35	2	250	0.8855	27	1.4745	—16.020°	Insol. 1:8–1:15
C	Sept. 18	Sept. 19	Partially mature herb	450	4	25	45	2	150	0.8747	18	1.4750	—16.919°	Insol. 1:8–1:15
D					4	25	53	2	70	0.8749	26	1.4783	—17.799°	Insol. 1:8–1:15
E					20	25	50–55	10	40	0.8648	12	1.4770	—18.809°	Insol. 1:8–1:15
10A					4	20	35	2	280	0.8982	26	1.4745	—14.523°	Insol. 1:8–1:15
B					4	20	40	2	275	0.8899	18	1.4740	—16.019°	Insol. 1:8–1:15
C					4	25	46	2	160	0.8858	19	1.4750	—15.624°	Insol. 1:8–1:15
D	Sept. 18	Sept. 19	Same character as No. 9	500	4	25	50	2	80	0.8887	18	1.4750	—15.574°	Insol. 1:8–1:15
E					4	25	52	2	50	0.9014	22	1.4780	—16.708°	Insol. 1:8–1:15
F					13	25	50–60	8	53	0.8967	20	1.4795	—15.970°	Insol. 1:8–1:15
11A					4	15	38	2	115	0.9522	60	1.4730	—8.0668°	Insol. 1:8–1:15
B	Sept. 18	Oct. 7	Same material as used in		4	20	45	2	215	0.9094	34	1.4735	—13.592°	Insol. 1:8–1:15
C			No. 10. Air-dried on		3½	20–25	55	2	65	0.8867	16	1.4740	—15.994°	Insol. 1:8–1:15
D			platform for 18 days	100	20	20–25	55–60	12	110	0.8684	25	1.4750	—14.543°	Insol. 1:8–1:15
12	Oct. 6	Oct. 7	Fairly well matured herb	325	36	20–25	50–60	26	550	0.9222	43	1.4740	—16.508°	Insol. 1:8–1:15

TABLE II—(Continued)

Lab. No.	Date of Cutting	Date Distilled	Character of Herb	Net Weight Pounds	Time Distillation, Min.	Pressure	Temp. Distillate	Distillate Gallons	Amt. Oil cc. Filtered	S. G. 25° C.	Ascaridol Per Cent.	Refractive Index 20° C.	Optical Rotation 25° C. 100 mm. tube	Solubility 70 Per cent. C_2H_5OH
13A					8	15–20	35	4	98	0.9470	56	1.4735	—13.518°	Insol. 1:8-1:15
B	Oct. 9	Oct. 10	Fairly well matured herb	350	3	20	40	2	100	0.9419	54	1.4733	—11.461°	Insol. 1:8-1:15
C					3	20	45	2	65	0.9389	50	1.4745	—7.370°	Insol. 1:8-1:15
D					18	20	45–50	14	110	0.9126	25	1.4750	—18.956°	Insol. 1:8-1:15
14A					3	25	30	2	145	0.9601	60	1.4735	—7.568°	Insol. 1:8—Sol. 1:15
B	Oct. 6	Oct. 17	Same as for No. 13. Air-dried for 10 days		3	30	45	2	270	0.9475	54	1.4730	—12.233°	Insol. 1:8—Sol. 1:15
C					3	30	50	2	80	0.9408	45	1.4730	—13.545°	Insol. 1:8—Sol. 1:15
D				170	12	30–32	50–55	8	70	0.9384	44	1.4750	—13.458°	Insol. 1:8—Sol. 1:15
15A					6	25–30	30	4	140	0.9302	44	1.4743	—15.065°	Insol. 1:8-1:15
B	Oct. 16	Oct. 17	Mature herb	350	4	30	40	2	63	0.9262	29	1.4760	—16.848°	Insol. 1:8-1:15
C					8	30	40–50	4	50	0.9075	21	1.4780	—13.878°	Insol. 1:8-1:15
16A					4	30	45	2	120	0.9536	57	1.4740	—8.273°	Sol. 1:15—Insol. 1:8
B	Oct. 16	Oct. 17	Mature herb	220	3	32	45-50	2	70	0.9498	57	1.4740	—10.674°	Insol. 1:8—Sol. 1:15
C					6	30	45	4	80	0.9351	45	1.4760	—16.200°	Insol. 1:8-1:15
17A					4	25	40	2	110	0.9273	43	1.4740	—16.791°	Insol. 1:8-1:15
B	Oct. 16	Oct. 24	Mature herb. Air-dried for 9 days		4	30	45	2	60	0.9244	35	1.4750	—16.843°	Insol. 1:8-1:15
C				180	8	30	45	4	45	0.9137	20	1.4750	—17.910°	Insol. 1:8-1:15
18A					7	25	35	4	90	0.9146	37	1.4752	—16.732°	Insol. 1:8-1:15
B	Oct. 23	Oct. 24	Mature herb	300	6	30	45	4	100	0.9121	28	1.4750	—21.433°	Insol. 1:8-1:15
C					17	30	45–55	12	50	0.8907	20	1.4770	—25.250°	Insol. 1:8-1:15
19A					3	30	40	2	95	0.9269	45	1.4750	—19.040°	Insol. 1:8-1:15
B	Oct. 27	Oct. 28	Mature herb	125	3	30	40	2	120	0.9250	40	1.4745	—15.138°	Insol. 1:8-1:15
C					9	32	40–45	6	90	0.9144	30	1.4760	—16.271°	Insol. 1:8-1:15
20A					4	30	40	2	240	0.9325	40	1.4743	—12.987°	Insol. 1:8-1:15
B	Oct. 27	Oct. 28	Mature herb	280	8	30	40–45	4	70	0.9259	38	1.4745	—18.498°	Insol. 1:8-1:15
21A					6	30	50–55	4	110	0.9559	62	1.4735	—15.373°	Insol. 1:8-1:15
B	Oct. 21	Oct. 22	Mature herb	300	17	30	50–55	12	125	0.9264	38	1.4760	—17.479°	Insol. 1:8-1:15

1924 Distillation Report

The following chart represents a summarized statement of the data as secured throughout all stages in the development of the 1924 herb, in relation to the production of the essential oil.

As will be noted the first cutting was made on July 21, the first distillation being conducted on the following day. The final cutting and distillation were conducted on October 27 and 28 respectively.

Analysis of the above chart would seem to indicate the following:

1. The entire lot of oils as secured from the 1924 herb failed to comply with the requirements of the U. S. P. IX in relation to the alcohol solubility requirement. In every case but two, they were also insoluble in fifteen volumes of 70 per cent. alcohol. No explanation of this behavior presents itself at this time, in view of the fact that the figures for Specific Gravity and Ascaridol percentage would indicate that the materials naturally ought to comply with this test. A chemical study of the alcohol insoluble portions no doubt would offer an explanation for this deviation from the results as obtained in the past.

2. The non-flowering plants yield but a trace of oil, the early flowering a slightly greater yield, the maximum yield being obtained just previous to or at the time of pollination, with a gradual decrease as the plant reaches maturity.

3. Ascaridol percentages were obtained ranging from 2 to 62 per cent. the former from plants in the early stages of flowering and the latter from the fully matured herb.

4. The greatest portion of the oil is received during the first five or ten minutes of a distillation run. Fifteen minutes appears to be a satisfactory average distillation period.

5. Although ascaridol represents the heavier fraction of the oil, the greatest yield is obtained during the first five or ten minutes of the distillation period. Two explanations present themselves for this phenomenon; (1) That ascaridol is readily carried over in steam distillation and (2) that on continued distillation a decomposition results as has been shown by other investigators.

6. Air-drying of the herb apparently results in an increase of the ascaridol content (Nos. 11 and 14). Note: Owing to a change in the Campus plans of the South Dakota State College, a portion of the 1924 wormseed plot had to be relinquished, thereby affording more material than called for in the original plans. Two sets

of distillations on air-dried material were conducted in order to utilize this excess material on hand.

7. In relation to the Optical Activity requirements, but four of the oils would comply with the U. S. P. Many strange and unaccountable deviations from the past were encountered in connection with the optical properties of the 1924 oils. The writer wishes to add at this point, that in many of the cases, the figures are but approximations, as many of the samples were quite dark in color and which did not permit for accurate observation in 100 mm. tube.

III. THE ORIGIN, NATURE AND PHYSIOLOGICAL ROLE OF THE ESSENTIAL OIL

Although much excellent work has been accomplished in connection with the chemistry of the Oil of American Wormseed, very little attention has been devoted to the micro-chemistry of this valuable anthelmintic plant.

The present investigation has proven to be of great value to the writer in the interpretation of some of the many difficulties previously encountered in the routine mechanical process of steam distillation of the herb. To illustrate one instance, it was the microscope that first revealed the fact that the greatest yield of oil was to be received just previous to or at the time of pollination. By means of the microscope and micro-chemical methods one is afforded the opportunity of noting the development of the oil within the plant itself, which type of study offers many possibilities to the commercial producer of essential oils. The commercial producer could well afford to employ micro-chemical studies of this character in conjunction with progressive series of distillations, for by so doing a rational procedure would be adopted as to the proper time of distillation, etc.

The plant physiologist of the past was primarily interested in the problem at hand, chiefly from the angle of a pure science study, and was not chiefly concerned with the economic interpretation of his findings. No doubt there is much valuable data secreted in the archives of the plant physiologist, which if an economic interpretation of same could be applied, it would offer the commercial producer of essential oils considerable in the way of rational explanation of the questions at hand.

Again work of this character entails considerable expense in the conduction of semi-commercial studies, for a vast amount of material must be available as well as suitable equipment for the proper han-

dling of the materials at hand. In many cases both types of facilities are not afforded the investigator, so that only one phase of the question is studied, thereby losing the great value of a parallel investigation, whereby both interpretations are not brought to a common point, with the result that much is lost which otherwise could have been gained by employment of both types of investigations.

Precautionary Measures

The present paper dealing with the Origin, Nature and Physiological Role of the Essential Oil, was not primarily intended as such, but rather an investigation to aid in an understanding of the problems connected with the semi-commercial production of the essential oil. However as the work progressed it naturally involved that implied in the title of this part of the paper, for one could not conduct the primary type of investigation without noting the various steps involved in the latter.

The writer realized at the outset of this investigation dealing with the problem of the origin, nature and function of plant secretions that the field of endeavor offered much in the manner of elusiveness and complexity. One but has to review the literature dealing with this subject wherein much has been written as to the manner of elaboration of essential oils, resins, etc., and also that there appears to be much in the way of varied opinions in regard to this matter.

One readily appreciates the fact that it is very easy indeed to arrive at a set of false conclusions, although apparently convinced in his own mind as to what appears to be the correct solution to a problem of this nature. In view of the above statements the writer wishes to emphasize the following as a forerunner to the work covered in the section dealing with Original Investigations.

1. That the findings, or rather a series of observations as submitted in this paper, are submitted only as a series of observations and not as a set of positive statements.

2. That in the study of plant secretions one must be fully cognizant of the individuality of the problem at hand, in that the mode of secretion is not to be looked upon as the same in all cases, but rather constitutes a matter of specificity.

3. That in view of the fact that a cell is a well organized and complex organic chemical laboratory, one must be fully cognizant

of the fact that secretion is a matter of chemical reaction as well as the processes involved in the morphological doctrine.

4. That the living cell, as soon as it is tampered with in any shape or manner, undergoes various changes, whereby the normal metabolic processes are altered, or made to cease entirely.

5. That at their best, micro-chemical methods are arbitrary and which are greatly influenced by many factors which necessarily must be taken into consideration.

6. A consideration of the physico-chemical nature of cell membranes.

7. Careful observations of a possible so-called "resinogenous layer."

8. That the drawings showing various changes involved in the development of the glandular hairs be accompanied with in so far as possible by photomicrographs to serve as a check on the former.

Original Investigations

A detailed study of all parts of the American wormseed plant throughout all stages in its development, confirms the statement by Wirth that the essential oil resides in the glandular hairs, which for the most part are located on the upper half of the ovary, in a dense ring-like formation (Plate 5). Contrary to the work of Wirth, the writer finds glandular hairs on the stems, especially on the younger types of stems. Wirth no doubt conducted his morphological studies upon mature stem material, where it has been noted that the hairs are few in number or may be absent entirely.

The hairs were noted on both sides of the leaf, being more abundant on the lower surfaces, especially on the smaller leaves of the flowering branches. They were also noted to be present in large numbers on the meristematic apices of the young seedlings and on the embryonic flower tips. They are practically absent on the woody basal portions, which accounts for the fact that steam distillations of these portions net but a mere trace of oil.

Description of Glandular Hairs

The hairs were noted to consist of three well-defined areas, *viz.*, (1) a stalk of rather thick-walled cells, usually of four or five cells, but which may vary at times, for the maximum number noted by the writer was fifteen (Plate 3, fig. 4B; Plate 2, fig. 5); (2) a chlorophyllaceous or secretory apparatus, consisting of one to three

cells (Plates 2, 3 and 4); a one-celled bladder-like cell or vesicle (Plates 2, 3 and 4).

Wirth has described the structure adjacent to the bladder-like cell as consistsing of one cell, but which as mentioned above has been noted to consist of one to three cells (Plate 3, fig. 4A). Wirth evidently made a study of the hairs in the final stage of development, at which time the cross walls have been absorbed in the developments that have taken place in the elaboration of the essential oil.

Paschkis has described the hairs for (*Chenopodium anthelminticum* L) which is evidently the same as *C. ambrosioides anthelminticum* Gray, as possessing a one to two-celled stalk, upon which strongly compressed from above is a moderately thin-walled capitulum, or more correctly a vesicle, which again would apply to the fully developed hair as described by Wirth, and which fully agrees with the findings of the writer for the fully matured hairs.

Numerous irregular-shaped bodies of unknown origin, nature and composition and function were noted in the chlorophyllaceous portion of the glandular hairs (Plate 3, fig. 3B). These are possibly bodies of a similar nature as described by Tunmann as being present in glandular hairs and which he thinks may consist of tannin (?) or fat (?). These bodies as reproduced in the plates are much inferior in distinctiveness to those in the original photographs.

Changes Involved in the Development of the Glandular Hairs With the Corresponding Formation of the Essential Oil

It was found to be very difficult, in fact next to impossible to differentiate between the glandular and non-glandular types of hairs in the earliest stages of development. The earliest recognizable type of glandular hair was noted to be one or two celled in structure containing cytoplasm, nuclei and vacuoles. (Plate 2, fig. 1.)

The bodies of unknown origin, nature and function soon make their appearance, but which later disappear entirely as the hair undergoes the various changes in the formation of the essential oil. The vesicular area and secretory portion of the glandular hairs are not sharply defined in the earliest stages of development. The chlorophyllaceous area soon assumes a greenish tinge, especially along the peripheral portions, the vacuolate areas becoming more distinct (Plate 2, fig. 2; Plate 3, fig. 2). This area soon assumes a deep green color becoming filled with a dense mass of plastid and other materials, the

cell or cells comprising this portion of the hair assuming a spheroidal or cup-shaped form. (Plate 3, fig. 3; Plate 2, fig. 3; Plate 4.) The nucleus assumes an abnormally large size, while the nucleus of the vesicular cell soon disappears entirely.

Shortly after the chlorophyllaceous or secretory portion has become densely filled with plastids and other materials, a most interesting reaction ensues, whereby numerous highly refractive yellowish-green oily globules make their appearance in among the green plastid material. This appears to be in agreement with Haberlandt under "Theoretical Consideration of Secretion Theories," wherein he states that "Numerous highly refractive vesicles and globules of various sizes make their appearance in the protoplast both before and during the process of secretion."

Pressure upon the cover glass at this stage in the development of the glandular hairs forces numerous oily globules into the large vesicular area and which respond in a positive manner to the 5 per cent. alcoholic KOH test (Wirth) (Plate 2, fig. 4).

The yellowish-green oily masses increase in amount with a subsequent slight yellowish-green coloration of the vesicular area, the entire area responding in a positive manner to the alcoholic KOH test.

A rapid decomposition or distintegration of the chlorophyllaceous material then takes places, and in place of the well-defined secretory area, one notes large globular masses of yellowish-brown or greenish-brown oil, while the remainder of the hair is filled with an oil of a light green color. (Plate 2, fig. 5; Plate 3, fig. 4.) A partial absorption of the cross walls has taken place by this time.

What appears to be the so-called resinogenous layer may be noted at times just previous to or at this stage in the development of the glandular hairs, at the base towards the rear of the cells that constitutes the cells of the secretory apparatus (Plate 2, fig. 5). This is better observed if hairs be cleared in successive strengths of hydrated chloral solution according to the method of Tunmann, utilizing hair material which has entered upon the stage of disintegration of the chlorophyllaceous area, up to the present stage of development.

The cross walls disappear entirely and the large oily globules or masses coalesce with the remainder of the oil in the hairs, with the result that one notes a single bladder-like cell filled with a light-greenish-yellow colored oil (Plate 2, fig. 6; Plate 6).

In the study of the hairs on the upper half of the ovary, these changes are complete for the most part just previous to or at the time of pollination. This observation suggests the idea that the function of the oil is that to serve as a protective ring against excessive transpiration and also as an attraction for insects. The greatest yield of oil is to be obtained by steam distillation at this period in the development of the herb.

Similar observations were noted in the case of the glandular hairs on the meristematic apices of the young seedlings, as well as in the case of embryonic flowering portions. The ovary, meristematic apex and embryonic flowering tips afforded the best material for the study of the changes involved in the development of the glandular hairs, for in all three one was able to discern all stages in the development of the hairs in large numbers.

No great change was noted in the hairs following that of the period of pollination, except that there was a decrease in size and many became wrinkled and broken, and as a rule were fewer in number on the upper half of the ovary in the final stages of development.

A similar brownish coloration was obtained as in the case of the hairs with alcoholic KOH in the examination of the pollen grains. It is possible that the pollen grains contain a small percentage of the essential oil, but it is more probable that this coloration is due to other constituents, possibly some forms of protein. A considerable amount of pollen has been collected for future chemical examination.

According to Garrigues the essential oil is present in the seeds but which is contradictory to the findings of Wirth. The writer has obtained a brownish coloration similar to that for the glandular hairs employing the alcoholic KOH test in the endosperm cells of the seeds. The ovaries and seeds were allowed to remain in the alcoholic KOH solution for several hours, during which time the brownish coloration developed. If allowed to remain for twenty-four hours a deep brown color was produced, but with a clearing of the glandular hairs. This reaction in the endosperm cells is probably similar in nature to that obtained for the pollen grains. The writer is of the opinion that the seeds do not contain the essential oil.

The decrease in the amount of oil after the period of pollination may be explained on the basis of vaporization, mechanical injury, a possible condensation or polymerization (?) of the organic constituents resulting in an increased percentage of ascaridol, and a corresponding decrease in the lighter fractions of the oil.

Summary

1. A parallel investigation of the American wormseed has been reported upon, in which the microscope and micro-chemical procedures have been brought in to play along with that of the routine process of steam distillation.

2. The investigation extended over a period of two seasons, beginning with the study of the young seedlings and continuing through the final stages of maturation.

3. The various lots of the essential oil of American wormseed as received from the 1924 plantings failed in every case to comply with the requirements of the U. S. P. IX.

4. The distillations were conducted for the most part on fresh herb, which no doubt accounts for the failure to secure a standard oil.

5. The 1924 report as embodied in this paper substantiates in part the findings for 1923, especially in that the non-flowering plants yield but a trace of oil; those in the early stages of flower formation yield considerably more but which is very low in ascaridol content. The greatest yield of oil is to be obtained just previous to or at the time of pollination, but again this oil is deficient in ascaridol content. To secure the maximum yield of ascaridol the herb should be fully matured and air-dried.

6. The essential oil no doubt serves as a protection to the plant by lowering of transpiration. It may also serve the function of attraction of insects for pollinating purposes.

7. The essential oil is apparently secreted by a "resinogenous layer" however at the expense of the cell contents.

8. The greater portion of the oil is obtained during the first five- or ten-minute period of a twenty-thirty minute distillation run, the first fractions containing the highest percentage of ascaridol.

9. Air-drying of the herb indicates an increase in the ascaridol yield over that obtained from the fresh herb.

10. Similar parallel studies should be conducted upon many of our valuable volatile oil-bearing plants, in order to ascertain the proper time of distillation.

11. The present standards as set forth in the U. S. P. IX for *Oleum Chenopodii* are indirectly based in some cases upon the percentage of ascaridol. In view of the fact that ascaridol has not been conclusively shown to be the active anthelmintic constituent of the essential oil, there needs be a careful consideration for a possible revision of our present standards.

Oleum Chenopodii U. S. P. X

The manuscript for the present paper had been practically completed when the Tenth Decennial Revision of the United States Pharmacopœia made its appearance. It is noted that a requirement of not less than 65 per cent. of ascaridol has been included in this revision for *Oleum Chenopodii.* Although not stated as such in the Ninth Decennial Revision, the requirements for *Oleum Chenopodii* in this revision practically embodied the same as set forth in the U. S. P. X, for the specific gravity constant is directly based upon the percentage of ascaridol present in the oil.

In view of the fact that ascaridol has not been definitely shown to be the active anthelmintic component of *Oleum Chenopodii,* it would seem that the present standards for this oil should be thoroughly investigated in the interim before the U. S. P. XI becomes officially accepted.

Let us ask ourselves the question "How has this requirement been established, when there is but very little, if any, evidence to support this official requirement?" We may also ask ourselves as to the reason why the past standards called for an oil which indirectly referred to an oil with a high percentage of ascaridol. Going back still further it would be an interesting fact to ascertain just why the distillers have always utilized the fully matured herb for the production of this valuable anthelmintic oil, in place of utilizing the herb in the flowering condition. Possibly it is due to the fact that from a purely empirical point of view we are generally apt to associate the strength of a vegetable product with that of "the fully grown" or "the ripe," etc., and apparently fail to realize that possibly more potent products are to be obtained from plants before they become fully grown or ripe.

At least it would appear so that in the case of the essential oil of American wormseed, that the present standards have been largely established upon empirical data and not upon rational or scientific facts.

As stated by Hall, it would be an interesting fact to ascertain whether his findings can be verified, in that the lighter fractions of the essential oil of American wormseed are less irritant and even more anthelmintic than the heavier fractions, the latter no doubt corresponding in a large measure to ascaridol itself. If the findings of Hall can be verified, then it would appear as though our present standards for this essential oil are just the reverse of what they

should be, for if such be the case, then the thing to be desired is an oil free or practically free from ascaridol.

According to the findings of the writer, the proper time of distillation should then be during the flowering stages of the plant, for from the flowering plants one obtains an oil low in ascaridol with the additional advantage that the yield of oil is considerably more than from the fully matured herb.

To extend this discussion somewhat further, it would again be interesting to ascertain whether or not p-cymene possesses any anthelmintic properties, for it has been shown that this substance is present in large amount in the lighter fractions of the oil. If such be the case it would be unnecessary to resort to the American wormseed plant for the substance that possesses the anthelmintic properties in question.

Acknowledgments

The writer wishes to especially thank Mr. D. F. Jones for the kindly interest which he has taken in the problem during the past five years as well as for financial assistance rendered which made possible the development of the work as presented at this time.

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Thanks are also extended at this time to the Director and his associates of the Department of Rural Journalism and Printing, South Dakota State College, for the many suggestions, etc., received in connection with the preparation of the color prints.

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EXPLANATION OF PLATES

PLATE 1. Tinted photomicrograph of pistil (immediately previous to pollination of flower) treated with 5 per cent. alcoholic KOH solution (aldehyde free), showing the localisation of the oil in the numerous glandular hairs, which are located on the upper half of the ovary in a dense ring-like formation. The scattering of the hairs is due to mechanical injury in preparation of the mount. Numerous pollen grains may also be noted, which have responded in a similar manner to the alcoholic KOH test.

PLATE 2. Tinted sketches of actual hairs noted showing the various stages in the development of the glandular hairs and a corresponding formation of the essential oil.

PLATE 3. A tinted photomicrographic study of several stages in the development of the glandular hairs.

PLATE 4. A tinted photomicrograph of two glandular hairs from lower surface of a leaf, showing the three well-defined areas, *viz.*, (1) stalk; (2) chlorophyllaceous or secretion area; (3) single large bladder-like cell or vesicle.

PLATE 5. A tinted photomicrograph of a single pistil just previous to pollination period of flower, depicting several stages in the development of the glandular hairs.

PLATE 6. A tinted photomicrograph of a single pistil taken from flower some time after pollination, showing the final visible stage in the development of the glandular hairs. Ovule partially protruding owing to pressure applied to cover glass. Numerous hairs are missing due to mechanical injury in preparation of the mount.

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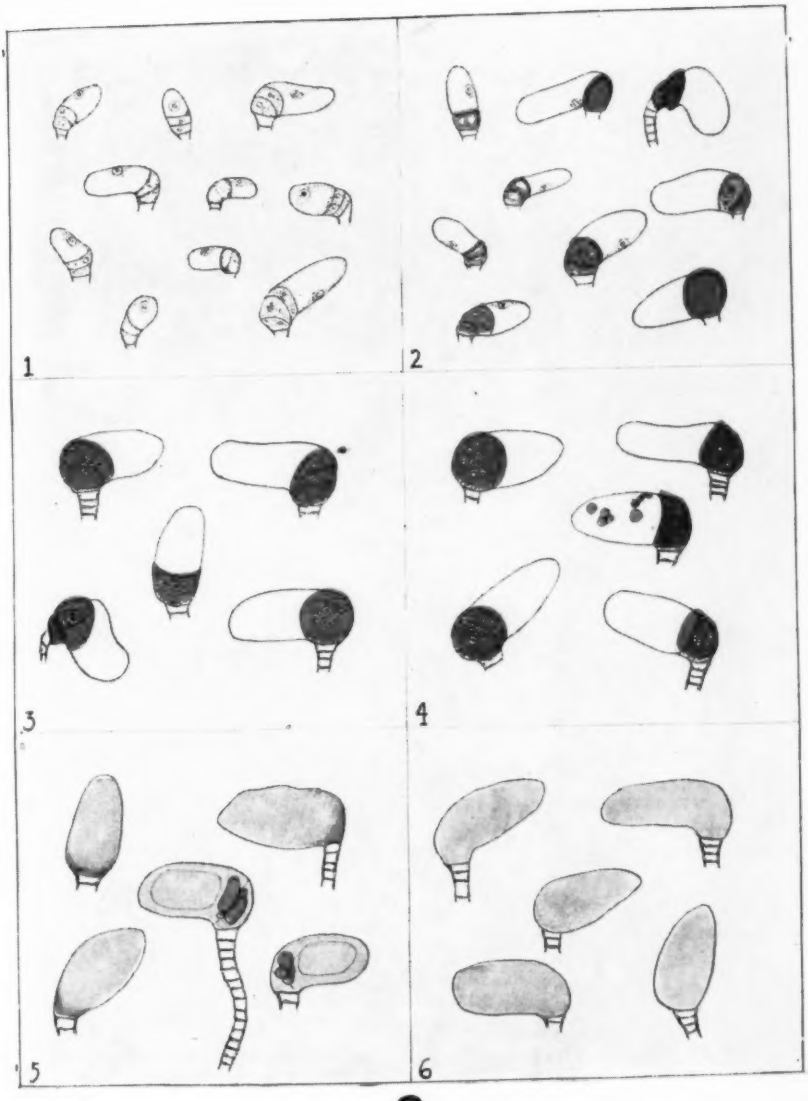

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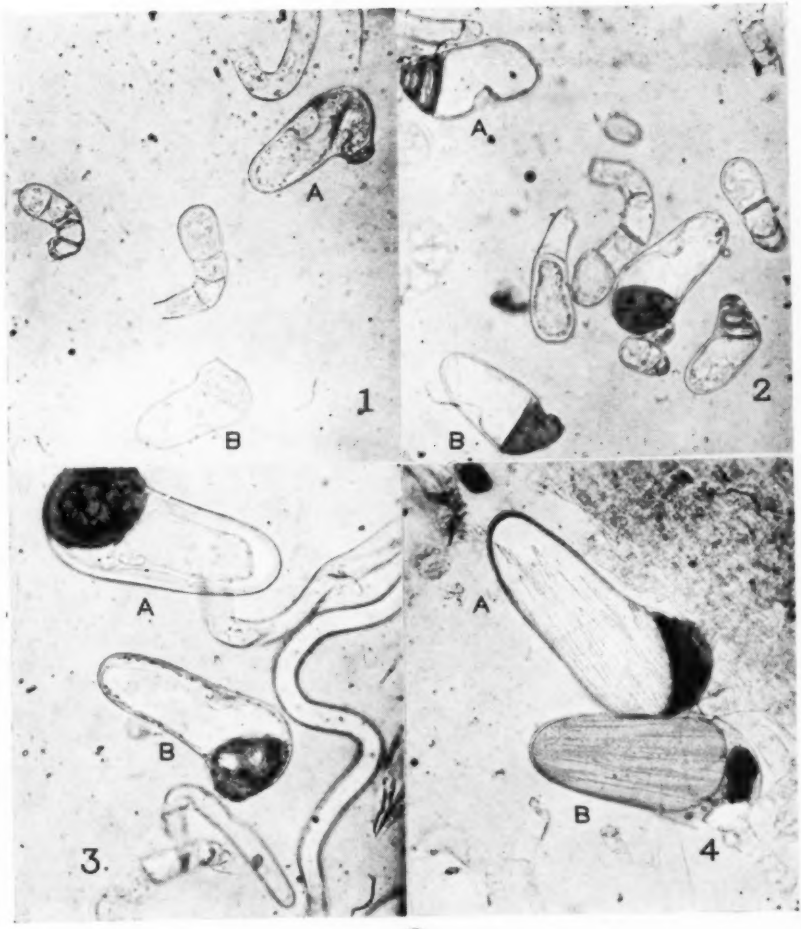

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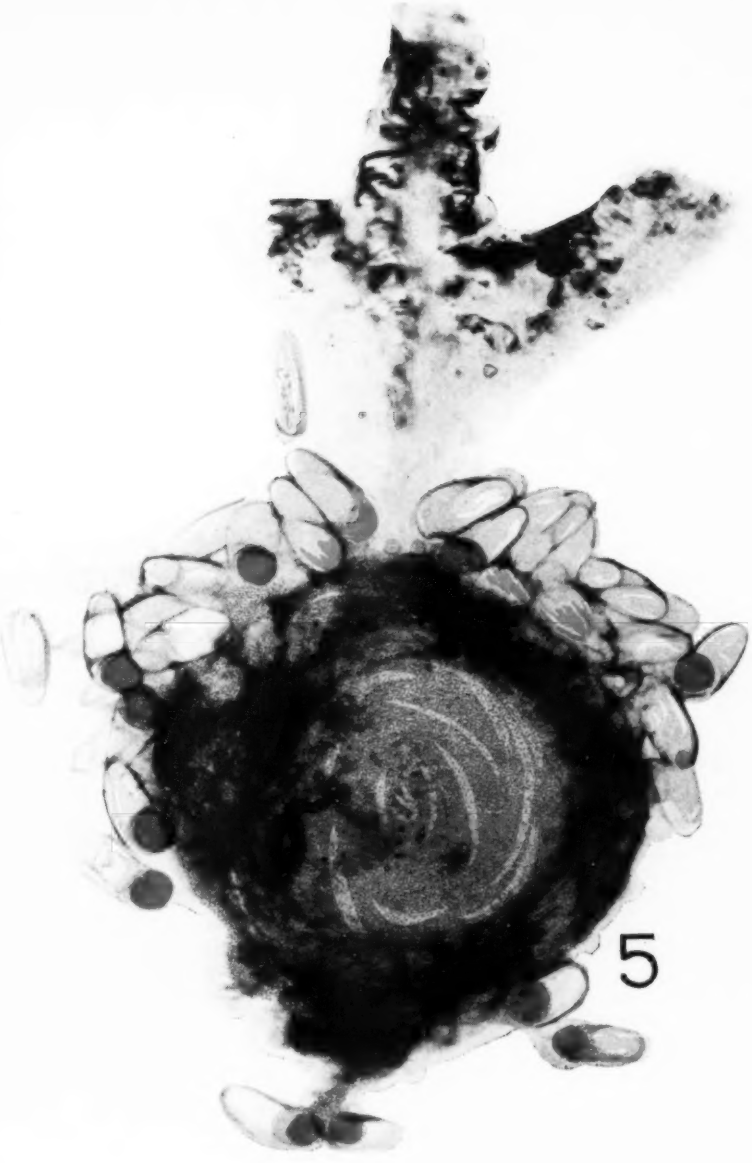

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ABSTRACTED AND REPRINTED ARTICLES

In re VITAMINS

(Abstracted From a Lecture by J. C. Drummond, Journ. Roy. Soc. Arts, March 12, 1926, p. 369.)

REPRODUCTION and rearing of young proves to be the exception rather than the rule among animals on a highly purified diet supplemented by Vitamins A and B sufficient for normal health and growth. In order that a species may also show normal reproductive capacity a further factor, Vitamin E, must also be present in the diet. Vitamin E has been found associated *only* with vegetable fats, for example abundantly in wheat oil.

Prevention or cure of rickets can be accomplished if a factor, Vitamin D, is present in the diet. Vitamin D resembles the more familiar Vitamin A in its natural distribution in both plant and animal tissues and in its general properties. It is distinguished from Vitamin A by its greater resistance to oxidation. Food mixtures deficient in Vitamin D become antirachitic upon exposure to ultra-violet radiations. Exposure to ultra-violet light rapidly cures rickets in children without change of diet. Acting upon cholesterol or phytosterol, ultra-violet light produces substances having a profound influence upon the calcification processes in bones. The nature of the photochemical change that occurs is unknown, but cholesterol itself unaltered cannot replace the vitamins in diet. This is the first instance where a vitamin has been prepared artificially in the laboratory from a substance readily obtainable in large amounts in pure condition. Our present belief is that exposure of the surface of the skin to ultra-violet radiations brings about a synthesis from cholesterol of the antirachitic vitamin.

In fats, it is not the glycerides but it is the *unsaponifiable residue* that contains the Vitamins A, D and E. It is also the non-saponifiable fraction of an inactive oil, like linseed oil, in which antirachitic potency is excited or produced by ultra-violet radiations. The vitamins in the unsaponifiable residue from cod liver oil are able to withstand temperatures as high as 200°C., and appear in a fraction distilling from the total unsaponifiable residue at temperatures between 180 and 200°C. at 1 to 2 mm. pressure. As the unsaponifiable residue is only about 1 per cent. of the original cod liver oil, it is

necessary to start with large amounts of the oil in preparing this active fraction. This active fraction seems to consist to a large extent of unsaturated alcohols.

Although no vitamin has yet been isolated in chemically pure condition, it is interesting to compare the smallest effective dosages of vitamin concentrates per 100 grams of body weight:

Concentrate containing	*Grams needed per 100 grams body-weight*
Vitamin A	0.00001 gram
Vitamin B	0.000027
Vitamin C	0.00015
Vitamin D	0.0001
Vitamin E	0.00025

These figures represent only the roughest approximations, but they are all of the same order.

The ratio between the two sexes seems to be profoundly disturbed, at conception, by deficiencies in Vitamin B in the previous diet of the male parent. The proportion of males decreases both with the degree of deficiency and with the time on the diet. This is illustrated by the following figures obtained by mating abnormally nourished males with normally nourished females, after the first month of incomplete nourishment:

SEX RATIO OF CONCEPTIONS

Diet	*Males*	*Females*	*Total*	*% Males*	*Probable Error*
Completely deficient	0	0	0		
Deficient + 1% yeast	29	52	81	36%	+ 3.6
Deficient + 2% yeast	35	43	78	45%	+ 3.8
Deficient + 3% yeast	82	87	169	49%	+ 2.1
Deficient + 4% yeast	37	39	76	49%	+ 3.9
Normal diet	34	34	68	50%	+ 4.1

The current explanation for the typical paresis of the limbs of animals suffering from deficiency of Vitamin B is that the nerves themselves have been damaged. But microscopically the nerves often appear to be normal. It seems more probable that the oxidative activity of the tissue has been lowered. This is in accord with the facts (1) that birds suffering from a deficiency of Vitamin B exhibit a markedly reduced respiration, and (2) that their body temperatures are greatly lowered. Experiments still in progress tend to show that the requirements of higher animals for Vitamin B are quantitatively

related to the total amount of food catabolised in the body. Isolated tissues removed from beri-beri animals show a depressed vital activity, as will be seen from the following figures:

OXYGEN UPTAKE OF MUSCLE TISSUE

(Expressed in cu. mm. O_2 per gram per hour)

Description of animal	*Medium used in the test*	*Oxygen taken up*
Normal	Ringer's Solution	592.2
Mild beri-beri	Ringer's Solution	306.8
Mild beri-beri	Ringer's Solution + yeast extract	567.0
Severe beri-beri	Ringer's Solution	77.4
Severe beri-beri	Ringer's Solution + yeast extract	194.6

—(*Abstracted by David Wilbur Horn.*)

THE DETERIORATION OF DRUGS IN THE PHARMACY *†

By Norman Evers, B. Sc., F. I. C.

DEFINITIONS are sometimes more odious than comparisons, as we have recently learnt in the case of alkaloids, but if I may be bold enough to attempt a definition of deterioration in drugs it is this—an alteration which affects either the medicinal value, the appearance, odor, or taste of a drug in such a way as to impair its value either as a therapeutic agent or as a saleable article. This leads one to divide deterioration in drugs into two classes, namely, changes which are apparent to the senses, such as change of appearance, odor, or taste, and changes which can only be detected by chemical methods

Chemical Changes

The latter group of changes go on without any indication that anything is occurring. Loss of an important active principle may occur, and the pharmacist may be unwittingly selling or using an article which is below the official standard in that respect. I propose to deal this evening with the chemical changes which occur in drugs

*Paper communicated to the Evening Meeting of the Pharmaceutiical Society in London, on February 9, 1926.

†Reprinted from the *Pharm. Journal and Pharmacist.*

and galenicals during storage and the best means of preventing these changes. Deterioration due to insects, moulds, and other forms of life I will leave on one side. Theoretically, chemical change can always be prevented, and therefore it is theoretically possible to prevent all deterioration whatever. If a drug is kept sufficiently cold, out of contact with air or moisture, and in a hermetically sealed vessel, no change whatever will occur, and it will keep for ever. Unfortunately these conditions are not attainable in practice, and we have to compromise by storing drugs under the best conditions possible. Nevertheless, a knowledge of the type of change likely to occur will enable us to choose the best conditions for storage and to prevent avoidable losses in material and money. We cannot exclude air from a bottle which has to be frequently opened, but if it contains easily oxidisable material we need not close it with a badly fitting cork.

We will now consider the chief types of changes which are liable to occur. These are changes due to

(1) Oxidation.
(2) Loss of volatile constituents.
(3) Absorption of water or carbon dioxide.

These four types may be all set down to one cause—namely, exposure to the atmosphere.

In addition to these we have changes due to

(4) Hydrolysis.
(5) Change of reaction or hydrogen-ion concentration.
(6) The action of light or heat.
(7) Catalytic decomposition.

Deterioration may, of course, be due to more than one of these causes acting together, and further an alteration due to one cause may render a substance more easily affected by a second cause. For instance, phenolic bodies are more susceptible to oxidation when the reaction is alkaline than when it is acid.

Changes Due to Oxidation

The absorption of oxygen from the air is a frequent cause of trouble in pharmacy. A few examples of the most important changes due to oxidation will now be given.

FERROUS COMPOUNDS.—The administration of iron in the form of ferrous salts is considered to have certain advantages over the use

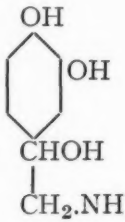
of the ferric compounds, and consequently we have several preparations in common use containing iron in a ferrous condition with other ingredients designed to preserve the iron from oxidation. The most common preservative is glucose as in Pil. Ferri B.P. or Syr. Ferri Iodidi, B.P. In the acid syrups such as Easton's Syrup, or Syr. Ferri Phosph. Co., B.P.C. syrup only is used, but as will be seen later, when we deal with changes due to hydrolysis, inversion of the sugar into glucose and lævulose proceeds rapidly on keeping, so that it is probable that the preservative action is due to the reducing nature of the glucose and lævulose rather than to the sucrose which, as you know, has no reducing action. In this connection it appears that it might be an advantage to prepare these syrups with invert sugar at the beginning, and so have the advantage of the action of the reducing sugars from the start. Hypophosphorous acid is also added in some cases, notably in Liq. Ferri. Iodidi Fort., B.P.C., in order to prevent oxidation, and proves very effective. In spite of the addition of these reducing compounds to iron preparations oxidation of ferrous salts is liable to occur if they are unduly exposed to the air. We are all familiar with the brown incrustation of ferric sulphate on ferrous sulphate crystals which have been kept for any length of time. Ferric phosphate is unfortunately less soluble in phosphoric acid than ferrous phosphate; consequently oxidation of the phosphate syrups results in the deposit of an unsightly precipitate. Mr. Frank Browne dealt with the B.P.C. formula for Syr. Ferri Phosph. Co. at the last meeting, and showed that a moderate increase in the acidity did not prevent the deposit. In Easton's syrup oxidation more frequently produces a brown coloration. Syr. Ferri Iodidi develops a brown color on exposure to the air owing to the formation of a ferric oxyiodide. This oxyiodide is said to be reduced again by sunlight to ferrous iodide. The addition of a small amount of hypophosphorous acid to this syrup effectually prevents oxidation.

ETHER.—Ethyl ether, after exposure to light and air, acquires a strong oxidising action, due to the formation of peroxides, to which the formulæ $C_2H_5O.CH(CH_3).O.OH$ and $CH_3.CHOH.O.O.CHOH.CH_3$ have been ascribed. These peroxides are the cause of undesirable after-effects when the ether is used as an anæsthetic. Middleton (Y.B.P. 1924, 615) has shown that the most important condition of storage is the exclusion of light, and that the amount of air in the bottle has little effect. If carefully purified at the start and

stored in amber glass bottles, little oxidation occurs, but the addition of 0.01 per cent. of pyrogallol has a powerful deterrent effect on the decomposition.

PHENOLS.—Nearly all phenolic bodies are susceptible to oxidation, and especially so when the reaction is alkaline. Phenol itself is liable to become pink on exposure to air. Pyrogallol, while stable in crystalline form, rapidly absorbs oxygen in alkaline solution with the production of a brown colour. Similar changes occur in the aminophenols which are used as photographic developers, such as amidol. Salicylic acid, which has a phenol group, is quite stable in the form of acid, and sodium salicylate is stable in solution provided that the reaction is not alkaline. If the latter is the case, oxidation occurs with the formation of a brown compound. For this reason commercial sodium salicylate always contains a slight excess of salicylic acid over and above that required to neutralise the sodium. The slight excess of acid makes it possible to keep solutions of sodium salicylate for a considerable time without alteration.

Adrenalin, which is l-methylamino ethanol catechol, contains two phenolic hydroxyl groups. Adrenalin solutions become pink on exposure to air, and the change is more rapid in neutral or alkaline solutions than in acid solutions.



VITAMINS.—Of the three vitamins of special importance in medicine, the growth-producing vitamin A, the anti-rachitic vitamin D, and the anti-scorbutic vitamin C all are extremely sensitive to oxidation. Cod-liver oil may lose a considerable proportion of its original vitamin A value in storage under conditions that permit oxidative changes. On the other hand, if properly stored out of contact with air, it may retain its activity for a considerable period. The bottle of oil shown has been stored for twenty years in a corked bottle with a lead cap, and still gives a color reaction for vitamin A as strong as some fresh oils. In the form of emulsion with malt extract or other emulsifying

agents, cod-liver oil retains its vitamin value for considerable periods. Since oxidation is the chief factor concerned in the inactivation of cod-liver oil and products containing that oil, it should, as far as possible, be stored with minimum exposure to air at as low a temperature as possible and in the dark. Oxidation of cod-liver oil accompanied by the development of an objectionable taste and smell in the oil. Vitamin C is equally sensitive to oxidation. The concentrated preparation from lemon juice may be stored in acid solution *in vacuo* for some months without loss of activity, but with access of air it loses its potency.

SALVARSAN or arsenobenzol and neosalvarsan or neoarsenobenzol are unstable in the presence of air, and in solution are rapidly oxidised with the formation of a yellow to reddish tinge and an increase in the toxicity. The powder is, therefore, stored in sealed tubes, and the solution is made immediately before use. Solutions may be kept under nitrogen gas in an ice-box for some months without change, but even in the presence of nitrogen a change occurs at room temperature.

ALDEHYDES.—A class of readily oxidisable compounds which will occur to the mind is the aldehydes. Of these the most important in pharmacy are formaldehyde, benzaldehyde, and cinnamic aldehyde. Formaldehyde in solution is slowly converted into formic acid $H.CHO + O = HCOOH$. The more important change that occurs in formaldehyde solutions is polymerisation with the formation of paraformaldehyde, which is slowly thrown out of solution. Polmerisation is retarded by retaining some methyl alcohol in the product.

Benzaldehyde is slowly oxidised to benzoic acid, and crystals of the latter may sometimes be seen at the bottom of old specimens or in essential oil of almonds. The same change goes on in cherry laurel water, which contains benzaldehyde. This change may cause trouble by inducing irritating properties if the water is used in eye lotions.

Cinnamic aldehyde is, as you know, the chief constituent of the essential oils of cinnamon and cassia. Oxidation to cinnamic acid may take place in the oil itself, and is particularly liable to occur in cinnamon water. The cinnamic acid may even form crystals in the water. A further decomposition may occur if the solution becomes mouldy, with the formation of cinnamene and styrene, which gives a benzene-like odour to the cinnamon water. Coumarin may also be

formed by conversion of cinnamic acid into o-hydroxy cinnamic acid, which by losing a molecule of water forms coumarin.

Another form of deterioration in which oxygen is concerned is the rancidity of fats. The development of rancidity is a complicated phenomenon, which is due, in the absence of bacteria, either to the action of air or to light and moisture on the unsaturated fatty acids which yield aldehydes and acid, but fats containing saturated fatty acids are oxidised in the presence of moulds to methylalkyl ketones thus:—

$$\begin{matrix} R.CH_2.CH_2.COOH + O \longrightarrow R.CHOH.CH_2.COOH \longrightarrow R.CO. \\ CH_2.COOH \quad \text{fatty acid} \end{matrix} \longrightarrow R.CO.CH_3 + CO_2.$$

Hydrolysis

Under this heading we include all changes due to chemical reactions brought about by the addition of water. The hydrolysis may be, as in the case of acetylsalicylic acid, a straightforward chemical reaction, or it may be induced by the action of enzymes, as in the destruction of digitalis glucosides. The process of hydrolysis, particularly where the action of enzymes is concerned, is greatly affected by the reaction or hydrogen ion concentration of the solution—*e. g.*, the inversion which goes on in acid solutions of cane sugar, but not in neutral solutions, and the hydrolysing action of trypsin, which is only exerted in alkaline solutions.

Acetylsalicylic acid affords a simple example of decomposition due to hydrolysis. The action of water is represented by the following equation:—

$$\underset{\text{Acetylsalicylic acid}}{C_6H_4\begin{matrix}OCOH_3\\COOH\end{matrix}} + H_2O \longrightarrow \underset{\text{Salicylic acid.}}{C_6H_4\begin{matrix}OH\\COOH\end{matrix}} + \underset{\text{Acetic acid.}}{CH_3COOH.}$$

Acetylsalicylic acid will, if kept dry, remain in good condition for a considerable time, but if allowed to become damp or if heated readily decomposes. When suspended in water the hydrolysis proceeds rapidly, and even more rapidly in solutions of the salts. For this reason all methods of administering acetylsalicylic acid in solution, such as dispensing with sodium citrate, are valueless unless the solution is given immediately after preparation, since after a short time the solution will consist of a mixture of salicylate and acetate. The pres-

ence of decomposition in acetylsalicylic acid can be readily detected by the odor of acetic acid which develops, by the ferric chloride test for salicylic acid, or by the melting-point, which is lowered.

HYDROCYANIC ACID.—Aqueous solutions of hydrocyanic acid decompose slowly on standing, with the production of ammonium formate and a brown substance,

$$HCN + 2H_2O = H.COONH_4$$

The brown substance is possibly a polymer of the formula $H_2N.CH(CN)_2$ The decomposition is said to be retarded by the addition of a small amount of hydrochloric acid; it is accelerated by light and by traces of alkali. Hydrocyanic acid is therefore best kept in amber-coloured bottles of neutral glass in a cool dark place. The loss is much reduced by keeping in paraffin-coated bottles. Hydrocyanic acid may also be lost from solutions owing to its volatility. It should therefore be kept well stoppered.

GLUCOSIDES.—Generally glucosides are fairly stable compounds, but they are readily attacked by certain enzymes, which usually occur in the same plant. The action of the enzyme is one of hydrolysis, as in the case of the decomposition of amygdalin by emulsin—

$$\underset{\text{Amygdalin,}}{C_6H_{11}O_5.O.C_6H_{11}O_4.O.CH(CN)C_6H_5} + 2H_2O \longrightarrow C_6H_5CHO + HCN + 2C_6H_{12}O_6$$

If therefore the enzyme is not destroyed in the drug, hydrolysis of glucosides may occur. A notable instance of this is seen in digitalis leaves; hydrolysis of the glucosides proceeds unless the leaves are carefully dried and kept in a dry atmosphere. It has been shown that digitalis stored in stoppered glass bottles kept in a dark place, and containing not more than 1.5 per cent. of moisture, will lose little of its potency even after two or three years. On the other hand, with a moisture content of 5.6 per cent. the potency decreased in eight months by 27 per cent., and with 10 per cent. of moisture by over 35 per cent. The same decomposition proceeds in tincture of digitalis, which slowly loses its potency on storage. It has been suggested that the leaves should be treated with boiling alcohol in the preparation of the tincture in order to destroy the enzyme, but this does not appear

to have met with approval. The preparation of the tincture with stronger alcohol has no advantage, since, although the enzyme may not be soluble, the glucosides are not thoroughly extracted. Very little loss in strength occurs in the tincture for a period of nine months after manufacture, but thereafter deterioration is more marked. The infusion of digitalis loses its strength much more rapidly, and should not be used after three or four days. Tincture of squill shows a similar loss of potency, but it retains some degree of activity for a longer period than digitalis. Strophanthus glucosides are remarkably stable, and the tincture does not lose potency for many years.

ALKALOIDS.—Certain alkaloids, particularly those which are readily hydrolysed, are slowly decomposed on keeping in the form galenicals, with the result that the preparations become below standard. Among the preparations specially liable to diminution in strength are those of coca, conium, colchicum, ipecacuanha, sanguinaria, and veratrum. Among the most stable are preparations of nux vomica, aconite, belladonna, hyoscyamus, stramonium, opium, and gelsemium. It is desirable that preparations of the former drugs should not be kept longer than two years from the time of manufacture. There has been much discussion recently on the question as to a reduction in the morphine content of opium occurring on keeping. On the whole the evidence appears to favour the view that little or no loss takes place. Ipecacuanha preparations probably show a slow loss of alkaloid, but here again the evidence is somewhat contradictory. The solanaceous alkaloids are remarkably stable in their preparations. This is somewhat unexpected, as the alkaloids are readily hydrolised. I do not know of any evidence which indicates whether racemisation of l-hyoscyamine goes on in preparations of the drug. It is known that atropine (the optically inactive form of hyoscyamine) does not occur in the fresh drug, but is only formed in the process of extraction of the alkaloids. It is therefore extremely probable that this process continues in the preparations.

THE HYDROLYSIS OF SUCROSE IN SYRUPS.—Sucrose in acid solutions is slowly hydrolysed or "inverted" with the formation of dextrose and lævulose.

$$\underset{\text{Sucrose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Dextrose}}{C_6H_{12}O_6} + \underset{\text{Lævulose.}}{C_6H_{12}O_6}.$$

This reaction goes on even in strong syrups in which acid is present, such as Easton's syrup or Syr. Ferri Phosph. Co. In these syrups where the sugar concentration is high the removal of water by the inversion of the sugar causes a contraction of volume with a resulting increase in specific gravity. This inversion may go on so far that crystals of dextrose may actually separate. On the other hand, the abstraction of water may cause quinine acid phosphate to crystallise from the syrup. The crystallisation of the latter salt is fairly common occurrence in Easton's syrup. The crystals form fine needles which give a silky appearance to the syrup when it is shaken. Easton's syrup when properly made is very nearly saturated with regard to quinine acid phosphate. It requires very little disturbance of the conditions such as the use of a little too much sugar or the abstraction of water by the inversion of the sugar to cause the syrup to become supersaturated with respect to quinine acid phosphate. The syrup may remain supersaturated for some time, but once crystallisation begins it proceeds rapidly, and the whole liquid may become an almost solid mass of crystals. The crystals may readily be redissolved by warming. It is clear that in products such as the iron phosphate syrups which are in a condition of chemical instability, it is absolutely essential that the greatest care should be exercised not only in their manufacture, but in seeing that they are stored under conditions which will retard these changes as far as possible. Storage in a cool place and the least possible exposure to air is the best means of effecting this.

Changes Due to Loss of Volatile Constituents

This is one of the most important, if not the most important, causes of deterioration in drugs. Unfortunately, it is not always easy to prevent it. When a bottle containing such a volatile substance as ethyl nitrite has to be frequently opened, it is practically impossible to avoid loss of strength. The only thing to do is not to keep it in too large bottles, and to keep it really well stoppered when not in use.

Spt. Æther. Nit.—At one time Spt. Æther. Nit. was a favorite with the Food and Drugs Act authorities, but nowadays it is rare to see a prosecution for this preparation. This is partly due to the fact that the standard of the B.P. 1914 is lower than that of the B.P. 1898, and allows for some loss of strength. It has been shown that the loss is almost entirely due to volatilisation, and that 3 per cent. of the activity may be lost even in pouring from one bottle to another. Liq. Ethyl. Nit. B.P. is rather more stable than Spt. Æther. Nit. The

presence of glycerin seems to have some preservative action. Both preparations should be stored in amber bottles, since light is said to cause decomposition of the ethyl nitrite. Excess of acid in the preparation may also cause rapid hydrolysis of ethyl nitrite. It has been suggested that the addition of magnesium carbonate prevents the production of excess of acid and preserves the strength. The magnesium carbonate is filtered off when the spirit is required for use. The addition of a small amount of sodium sulphite is also said to act as a preservative, but the adoption of such means of preservation, of course, produces an article which is not strictly B.P. However well Spt. Æther. Nit. may be kept up to strength by care in storage, it is certain that it does not keep in mixture form, and the use of concentrated mixtures containing it is to be condemned. Recently I had occasion to examine a number of concentrated mixtures, and although they had been recently prepared, the amount of Spt. Æther. Nit. found was, on the average, about one-sixth of the amount added.

Amyl Nitrite glass capsules have been sometimes found to explode, but this does not occur unless water is present in the capsules.

LIN. CAMPHORÆ.—Contrary to many statements which have been made, camphorated oil does not lose in strength on keeping under ordinary conditions.

LOSS OF AMMONIA.—Preparations such as Tinct. Quinin. Ammon. and other ammoniated tinctures, in fact, all preparations containing free ammonia, are liable to losses due to the volatile nature of the ammonia. Messrs. Self and Corfield (*Pharm. Journ.*, Feb. 6, 1926, 134) have shown that powdered ammonium carbonate is liable to lose ammonia, and that the practice of keeping a solution of 1 in 8 strength is much less liable to errors on account of diminution in strength. This solution is perfectly stable when kept in stoppered bottles at ordinary temperatures, even when dispensed at frequent intervals. It was also shown that mixtures containing ammonium carbonate, when preserved for a month in ordinary corked bottles, showed not more than 2 per cent. loss.

OINTMENTS.—Ointments containing volatile constituents such as phenol ointment are liable to lose part of their potency on storage under ordinary conditions. Since there are no official standards for these ointments—that is to say, a manufacturing formula is given by the B.P., but no standard for the finished ointment, and as consider-

erable loss of volatile matter takes place in the course of manufacture—the comparatively slight losses that occur on keeping are not of great importance. The phenol in phenol ointment may crystallise if the ointment is subjected to great cold.

In the case of iodine ointment, loss of free iodine proceeds not so much from volatilisation as from combination with the ointment base. About 30 per cent. of the iodine added is absorbed during manufacture, and a further 5 per cent. goes into combination during the first month of storage. After that time it is a relatively stable preparation.

FORMALDEHYDE TABLETS.—Considerable losses of formaldehyde may occur in these tablets on keeping, and they should preferably be stored in airtight containers. It has been suggested that the use of paraformaldehyde in place of formaldehyde would prevent this loss, but there is some doubt as to whether this would be equally effective.

EFFLORESCENCE.—The loss of water from crystalline salts may be regarded as falling under the heading of loss of volatile constituents. When a hydrated salt such as sodium sulphate is placed in a perfectly dry atmosphere, it gradually loses water, and therefore exerts a vapor pressure. If the vapor pressure of a hydrate is greater than the vapor pressure of water vapor in the atmosphere, the salt will lose water—*i. e.*, will effloresce. This is the case, for example, with common washing soda, $Na_2CO_3.10H_2O$, which, when exposed to the air, loses water with the production of a lower hydrate. The vapor pressure of a hydrate increases rapidly with temperature. Thus, ordinarily sodium phosphate, $Na_2HPO_4.12H_2O$, has a vapor pressure at 25° C. of over 18 mm., which is greater than the average pressure of aqueous vapor in the atmosphere. The salt will therefore effloresce at 25° C. Sodium sulphate shows very similar behavior, and effloresces rapidly in a warm, dry atmosphere. Efflorescence assumes a practical significance in the case of bath salts. These crystals are hydrated sodium carbonate, and unless carefully kept in a cool place are likely to effloresce and lose their pristine beauty. It will be seen from these remarks why it is unwise to put bottles of bath salts in a shop window in full sunlight on a hot summer's day. In America sodium thiosulphate is often used for bath salts because it does not effloresce, and forms crystals of attractive shape.

Deterioration Due to Absorption of Water and Carbon Dioxide

While on the subject of efflorescence we may aptly consider the reverse process—deliquescence. Deliquescence is the absorption of water from the atmosphere by a crystalline salt. All deliquescent salts are very soluble in water, and this suggests an explanation of the change. A little saturated solution is formed by a trace of moisture condensed on the surface of the solid. The vapor pressure of this is less than the pressure of aqueous vapor in the atmosphere. Moisture is attracted by the salt which gradually liquefies to a saturated solution, which goes on absorbing moisture until its dilution is such that the vapor pressure is equal to the partial pressure of water in the atmosphere. Solids which attract water without liquefaction and liquids, such as alcohol and sulphuric acid, are said to be hygroscopic. Examples of deliquescent salts are potassium carbonate, calcium chloride, sodium iodide, and mercuric potassium iodide.

The case of calcined magnesia is interesting. The B.P. requires that this compound shall lose not more than 1 per cent. of its weight when heated to dull redness. This is a standard which is readily attained when the magnesia is made, and the heavy variety can be kept up to this standard under ordinary conditions of storage with little trouble. The light variety, however, is very much more hygroscopic, and it is probable that the standard of 1 per cent. is rather too severe. In order that the loss on heating may not exceed 1 per cent., light magnesium must be very carefully stored in well-stoppered bottles, and should not be allowed to lie about exposed to the air, as is often done. Carbon dioxide is absorbed by magnesia as well as water. This absorption goes on in Pulv. Rhei Co., and this preparation should also be stored in airtight containers. Other examples of difficulties due to the hygroscopic nature of materials are the absorption of moisture by sugar in the form of lozenges, pastilles, etc., causing them to become soft or to stick together.

Change of Reaction or Hydrogen Ion Concentration

Change of hydrogen ion concentration is chiefly to be considered as a cause predisposing to other changes, such as hydrolysis or oxidation. I have already mentioned the development of acidity in Spt. Æther. Nit. as a cause of hydrolysis of ethyl nitrite.

PEPSIN.—Pepsin in acid solutions will retain its activity for considerable periods, but even in slightly alkaline solutions it rapidly diminishes in potency. Preparations such as Elixir Bismuth. et Pepsin Co. are therefore based on unsound chemical knowledge, since the presence of Liq. Bismuth. causes them to be slightly alkaline, and, in fact, the pepsin after a short time is found to be a negative quantity.

Changes in reaction are often caused by the use of alkaline glass bottles or containers, and preparations which are sensitive to alkali should always be stored in bottles or ampules of neutral glass. This is particularly important when the solution is to be sterilised, since much more alkali is extracted from the glass when heated. Solutions of cocaine, novocaine and other local anæsthetics are readily decomposed by sterilization in ampules of alkaline glass. Changes of this nature may be often prevented by the addition of "buffer" solutions. Solutions of salts such as phosphates, borates, citrates, etc., have the property of resisting slight changes in hydrogen ion concentration. Probably the use of this device might be profitably extended in pharmacy. An instance where it has been employed is found in Dakin's solution, where the addition of boric acid to the solution of sodium hypochlorite prevents the development of acidity in the solution and the resulting decomposition of the hypochlorite.

INSULIN.—Insulin and other active hormones are peculiarly sensitive to the reaction of the solution, and must be kept in bottles of glass which is absolutely neutral. Insulin is prepared in a solution which is slightly acid at a pH of about 3.5. In this condition insulin will keep for long periods, especially if kept in cold storage. The introduction of a trace of alkali either from the glass or from a hypodermic needle which has been sterilised in lysol, which is alkaline, or even in alkaline tap water, may cause the insulin to become cloudy when the pH has been changed to about 4.5. In this condition the insulin is still active, but it retains its activity for a much shorter period than at a pH of 3.5. If more alkali is added the insulin redissolves and rapidly loses its potency.

PITUITARY EXTRACT shows a similar behavior, and retains its potency best at a pH of about 3.5. I have already mentioned the sensitiveness of adrenalin and other phenols to oxidation in alkaline solutions. The case of hydrogen peroxide will be dealt with later.

The Action of Light and Heat

All chemical changes concerned with the deterioration of drugs proceed more rapidly if the temperature is raised, and many chemical changes are accelerated by the action of light. Several reactions of the latter class have already been mentioned, and it is hardly necessary to mention that nearly all types of deterioration can be retarded by storage in a cool place. Provision of cold storage has been found a necessity by many wholesale houses with the extension of the use of animal products, sera and vaccines, and it is probable that in the future the retailer may also come to look upon it as indispensable. Exposure to cold may, however, induce crystallisation, essential oils may deposit crystalline constituents, or fixed oils may deposit "stearine." Cod-liver oil and liquid paraffin are both refined by filtration at a low temperature, so that no cloudiness should appear in these if not cooled below the freezing-point of water. Any changes due to exposure to cold can easily be remedied by warming up again, unless the bottles have burst through freezing.

Catalytic Decomposition

The classic example of this type of change is hydrogen peroxide, which on occasion adds to the excitement of life by turning the pharmacy into a realistic imitation of trench warfare. Hydrogen peroxide is peculiarly human in its qualities. It strongly objects to impurities in its system, and, like some people, it develops gas on the slightest provocation. It is responsive to the depressant action of drugs like acetanilide and quinine. Contact with alkaline glass or stone bottles upsets its stability. It keeps best when of the highest purity with a trace of acid, and a trace of some preservative, such as acetanilide or quinine. Decomposition is hastened by the presence of the merest trace of certain substances, particularly of certain metals.

Castor Oil.—Castor oil becomes darker in color and increases in acidity on keeping. The darkening in color appears to be accelerated under certain conditions. A few days ago I saw a tray of white glass bottles of castor oil which had all been filled from the same tank six weeks previously, and had been kept in a fairly dark room since. Whereas the large majority were of the usual pale yellow color, the oil in certain bottles had become very much darker in color. On the face of it, it appeared that the only possible cause of

the darkening was either some impurity left in the bottles or the glass of the bottles themselves. On pouring out the oil it was seen that the glass of the bottles containing the darkened oil was of a different color to that of the other bottles. Evidently something in the glass of the bottles must have accelerated the change, probably by acting as a catalyst. I have not yet had time to carry the investigation further, but this is a good example of the unexpected things that happen in pharmacy, and of the interesting problems which it is continually providing. The dark color formed in the oil may be again bleached by exposure to sunlight. The increase in acid value of castor oil, which is probably induced by bacteria, or an enzyme, may be so great that in a few months a good oil may no longer be within the B.P. limits for acidity.

Crystallisation

Crystallisation in Easton's Syrup has already been mentioned. There is one other instance which may be touched on, the crystallisation of maltose from malt extract or malt and oil. Sometimes crystals appear in tufts on the side of the jar and slowly grow until the whole of the contents is a solid mass. If the malt extract has been properly made, this should not occur within a reasonable time, but, particularly if the diastatic value is high, it may occur after a few years. As would be expected, crystallisation is hastened by storage at a low temperature.

Requirements for the Storage of Drugs

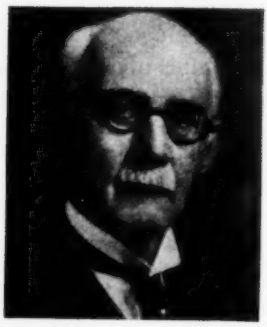
From what has been said, it appears that the requirements for the storage of drugs which are likely to deteriorate are comparatively simple. A minimum of exposure to air, well-stoppered bottles, a low temperature, and protection from light, are the ideals to be aimed at in nearly all the cases I have mentioned, and the nearer one can approach to these conditions in practice the more successful one will be in the avoidance of losses due to deterioration.

It has been my object this evening to put before you the chemical nature of some of the changes which go on when deterioration in drugs occurs, because, in my opinion, a knowledge of these changes cannot fail to be of practical value to the pharmacist who is faced with the task of preserving, often under difficult conditions, such a variety of unstable materials as is met with in pharmacy.

DR. FRANCIS E. STEWART

Testimonial Dinner

ON TUESDAY, March 23, 1926, the Faculty of the Philadelphia College of Pharmacy and Science, and other Philadelphia friends tendered to Dr. Francis E. Stewart, of Philadelphia, a testimonial dinner in recognition of his long and fruitful service in the advancement of professional and business ethics in connection with the manufacture and distribution of medicinal products.



Dr. Francis E. Stewart

Prof. C. H. LaWall acted as toastmaster, and speeches were made by Mr. Joseph W. England, chairman of the Board of Trustees of the Philadelphia College of Pharmacy and Science, Prof. J. W. Sturmer, Dr. Ambrose Hunsberger, Mr. Milton Campbell, president of H. K. Mulford Co., Prof. E. Fullerton Cook, Dr. W. W. McNeary, Dr. David Wilbur Horn and others.

The hosts of the occasion were the following:

Dr. and Mrs. Charles H. LaWall, Prof. J. W. Sturmer, Mrs. Sturmer, Miss Mary Sturmer, Prof. Freeman P. Stroup, Prof. and Mrs. E. Fullerton Cook, Prof. and Mrs. Arno Viehoever, Mr. Shinohara, Mr. E. N. Meuser, Dr. Horatio C. Wood, Prof. Louis Gershenfeld, Mr. Ralph Calvert, Mr. Paul Q. Card, Miss Ellen Cawley, Mrs. Cawley, Mr. L. G. Freeman, Mr. Thomas Githens, Mr. Hampton Hoch, Dr. David Wilbur Horn, Prof. E. J. Hughes, Prof. and Mrs. William B. Jackson, Mr. and Mrs. Howard Kirk, John E. Kramer, Mr. George N. Malpass, Mr. J. L. Nebinger, Dr. and Mrs. George D. Rosengarten, Mr. and Mrs. W. J. Stoneback, Mr. and Mrs. William L. Cliffe, Prof. and Mrs. Robert P. Fischelis, Mr. Ralph R. Foran, Mr. and Mrs. Richard Lackey, Mr. and Mrs. Joseph C. Peacock, Mr. and Mrs. Mahlon C. Kline, Mr. and Mrs. S. H. Whyte, Mr. Joseph W. England, Dr. and Mrs. Hunsberger and Ambrose Hunsberger, Jr., Mr. Joseph W. Harrisson, Mr. Jacob S. Beetem, Mr. Milton Campbell, Dr. Solis-Cohen, Mr. W. W. McNeary, Mr. L. G. Cordier, Mr. Harvey P. Frank.

Dr. Stewart is nationally known for his activity in behalf of pharmaceutical ethics and in harmonizing the interests of pharmacy and medicine, especially in the manufacture of medicinal preparations.

Dr. Stewart was born in Albion, N. Y., on September 13, 1853, and is a descendant of the Perthshire Stewarts. He was educated at Cortland County Academy, Homer, N. Y., and at Oberlin College, Ohio. He was graduated from the Philadelphia College of Pharmacy in 1876 with the degree of Ph. G., and immediately took up the study of medicine, graduating at Jefferson Medical College in 1879.

Later he took post-graduate work at the University of Pennsylvania. Following his graduation in medicine, he practiced for a time in New York City, where he occupied a number of important positions on medical committees and charity organizations. His specialty has been pharmacology, and the supervision of pharmacal and pharmaco-chemical industries by the United States Government has been his lifelong ambition.

From 1885 to 1891 he resided in Wilmington, Del., where he occupied a prominent position in the scientific and educational life of the community. From 1891 to 1894 he was connected with sanitarium work at Watkins Glen, N. Y. In 1894 he organized a scientific department for Frederick Stearns & Company, Detroit, Mich.

In 1898 he became chairman of the Medical Board of Merck & Company and editor of *Merck's Archives*. He then went to California and assisted in organizing the National Bureau of Medicines, which later developed into the Council on Pharmacy and Chemistry of the American Medical Association.

Following his graduation at the Philadelphia College of Pharmacy he was, for a time, a quiz master in pharmacy and chemistry for the Alumni Association. He has also occupied teaching positions in Jefferson Medical College and the Woman's Medical College.

Later he became professor of materia medica and botany and physiology in the Medico-Chirurgical College, and was awarded the honorary degree of Phar. D. in that institution in 1914. In 1916 he was made lecturer on pharmacy laws at the Philadelphia College of Pharmacy. He is at present consulting director of the Scientific Department of the H. K. Mulford Company.

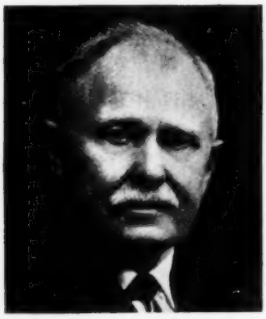
Dr. Stewart is a chairman of important committee in the Pennsylvania Pharmaceutical Association and other scientific bodies. He is a member of many important professional and scientific organizations and of the Masonic Order and an elder in the Presbyterian

church. He is the author of a quiz compend of Pharmacy, and is a frequent contributor to pharmaceutical and medical literature. He is a historian and life member of St. Andrew's Society of Philadelphia, has traveled extensively, and numbers among his professional and personal friends many leaders in medicine and pharmacy at home and abroad. His hobby is the study of patents and trade-marks as related to medicine and pharmacy and he is a recognized authority on this subject.

EMIL LOUIS BOERNER

An Appreciation

FIFTY YEARS as proprietor of the same retail pharmacy is the exceptional record of Emil L. Boerner, of Iowa City, Iowa, Dean Emeritus of the College of Pharmacy of the State University of Iowa.



Emil Louis Boerner

Professor Boerner was born near Siegen, Westphalia, Germany, April 21, 1855, the older of two sons of Henry William Boerner and Caroline Becking Boerner. When but two years old, his parents came to the United States and settled in Newtown, Pa., later moving to Chippewa Falls, Wisc. Here he received his early education in what were then frontier schools.

In 1867 the family moved to Iowa City, Iowa. He graduated from McLean's Commercial College and then worked for three years in the drug store of Thomas J. Riggs. He has the unique distinction of being the first clerk in Iowa City who did not wear a hat in the store.

He entered the Philadelphia College of Pharmacy in 1874 and two years later was graduated with high honors, receiving the degree of Ph. G. During his college course he worked in the store of William C. Bakes, Tenth and Arch Streets, Philadelphia; and during one summer he managed Mr. Bakes' store at Ocean Grove, N. J. His roommate in college was Albert H. Van Gorder, vice-president Hall-Van Gorder Company, Cleveland, Ohio.

The class of '76 had many who became prominent in their chosen profession, some of whom have passed beyond. Pharmacy owes much

to such men as Louis Emanuel, Carl S. N. Hallberg, William D. Robinson, Francis E. Stewart, Charles W. Tobey, Henry Trimble, Joseph L. Weber, Emil L. Boerner, and others like them.

Professor Boerner's graduation thesis was "Ricinus Communis." The process used today in the commercial production of castor, linseed and other fixed oils is the outgrowth of his original work.

On May 1, 1876, he opened a retail pharmacy in Iowa City, and has been its proprietor continuously for fifty years. While conducting his pharmacy he found time for other activities. From 1882-1884 he lectured in the Iowa College of Pharmacy at Des Moines. In 1885 he with J. H. Harrison and George H. Shafer, all three men prominent pharmacists and active in the work of the Iowa Pharmaceutical Association, constituted a committee that brought about the establishment of the Department of Pharmacy (now the College of Pharmacy) at the State University of Iowa. Professor Boerner was chosen professor of theory and practice of pharmacy and dean of the faculty, which position he held up to 1904.

In 1897 he organized the Boerner-Fry Company, manufacturers of perfumes and flavoring extracts, and was its president until 1908, when he withdrew from the company to devote all of his time to his retail store. Boerner's Prescription Pharmacy is known over the State of Iowa as a store that emphasizes the business of compounding prescriptions, drugs and medicines.

Professor Boerner was awarded the honorary degree of doctor of pharmacy by the State University of Iowa in 1896. He is a Rotarian. For nearly fifty years he has been an active member of the Christian Church. He is a life member of the Philadelphia College of Pharmacy and Science and of the American Pharmaceutical Association, joining the former in 1876 and the latter in 1877.

In 1883 Professor Boerner was married to Miss Helen Louis, of Iowa City, and they have two sons and one daughter.

E. S. R.

FACULTY OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE, 1926.

First Row (Upper)—J. L. Nebinger, T. L. Hynes, C. C. Pines, W. B. Jackson, Ellen Cawley, G. W. Perkins, G. N. Malpass, J. Kramer, J. H. Hoch.

Second Row—H. P. Frank, H. W. Kirk. C. F. Dapp, L. G. Freeman, J. L. Sigmund, L. G. Cordier, R. L. Calvert, P. Q. Card, T. B. Githens.

Third Row—G. W. Patterson, G. W. Rosengarten, P. S. Pittenger, E. J. Hughes, A. B. Nichols, I. Griffith, E. A. Mullen, C. E. Vanderkleed, M. S. Dunn, W. J. Stonebach.

Fourth Row—H. Leffmann, L. Gershenfeld, E. Fullerton Cook, F. P. Stroup, J. W. Sturmer, C. H. LaWall, F. X. Moerk, A. Viehoever, H. C. Wood, D. W. Horn, F. E. Stewart.

SCIENTIFIC AND TECHNICAL ABSTRACTS

SHELLAC WAX.—This wax is obtained in India by heating stick lac with water, cooling and collecting the wax which solidifies on the surface. By this method large quantities of the wax can easily be obtained, but it is possible that wax with higher melting point may remain in the stick lac. The following method of obtaining the wax was therefore adopted to insure the whole of it being separated: Indian stick lac was carefully separated from fragments of the twigs and bark, ground to a fine powder, and completely exhausted with water; this treatment removed sugar, proteid substances, soluble salts, coloring matter, etc.; the residue was then percolated with cold alcohol until no more resin was extracted and dried; the dried powder was next extracted with hot xylol and the solution allowed to cool, when the crude wax separated as a yellow mass. This is a mixture, part (80 per cent.) being soluble in hot alcohol and part insoluble. The alcohol-soluble portion—purified by decolorization with animal charcoal and recrystallization, formed a hard, colorless, brittle substance melting at 80°-81°. It can be saponified by long heating with alcoholic potash, and then yields the wax-alcohol and the potassium soap of the wax acid. The wax-alcohol was extracted by ether; it was decolorized by animal charcoal, recrystallized several times from alcohol and benzene and dried. The melting point was 79°, and the wax had the formula $C_{25}H_{52}O$. It is identical with the alcohol found by Damoy in beeswax and termed neoceryl-alcohol; as, however, Tochireb had already isolated it in 1923 and named it tachardiacerol, this name should be employed for it. The acid was isolated in the usual way from the potash soap; it melted at 78°, and had the composition $C_{25}H_{51}COOH$; it is possibly identical with cerotic acid. The portion of the wax that is insoluble in alcohol was similarly treated. It yielded an alcohol melting at 89°-90°, possessing the formula $C_{32}H_{66}O$, and identical with Gascard's laccerol. The acid with which this alcohol was combined was pale yellow in color, melted at 93°, and was identical with Gascard's lacceric acid, $C_{32}H_{64}O_2$. The crude wax also contained about 2 per cent. of a white hydrocarbon, tachardiacerin, $C_{25}H_{52}$, melting at 54°-55°.—Tschvich and Schäfer (*Pharmaceutica Acta Helvetiæ*, 1, 9), through *Pharm. Journal.*

ILLINIUM (ELEMENT No. 61).—Hail to illinium, chemical element number 61, first to be born on American soil. For Prof. B. S. Hopkins, of the University of Illinois, has isolated the hitherto unknown element 61 after detailed chemical work extending over several years.

Four hundred pounds of monazite residues, donated by one of the big manufacturers of gas mantles, yielded the new element only after this quantity of rare earth material had been subjected to repeated fractional crystallization. Professor Hopkins found it extremely difficult to separate the new element, illinium, from neodymium, another element, which masked its presence.

From theoretical considerations, physicists and chemists have predicted just what spectral flags, as it were, the new element should fly when it is detected with spectroscope and X-ray. And Professor Hopkins bases his claim of discovery on many new lines in the spectrum, prominent bands in the absorption spectrum in the expected position and lines in the X-ray spectrum in the predicted position.

The element is named after the university at which it was discovered, and its symbol will be the first two letters of its name, Il.

Little practical use for illinium can be predicted, as it is just another of a large family of very closely related and much mixed up rare earths. Some of these rare earth elements make up the incandescent part of gas mantles in everyday use, and it is probable that small amounts of illinium are actually contained in such mantles.

Now all but two of the ninety-two fundamental materials of the universe, the chemical elements, have been discovered. The two still missing are numbered 85 and 87.

Efforts to locate element number 87, called prenatally ekacæsium, have been made at Harvard by Prof. T. W. Richards and Dr. E. H. Archibald in 1902 and again by Prof. G. P. Baxter in 1915. All these experimenters made successive fractionations of cæsium nitrate and other cæsium salts. Element 87 is known to belong in the alkaline group along with sodium, potassium and cæsium. Later attempts were made by Prof. L. M. Dennis and Dr. R. W. G. Wyckoff at Cornell University, in 1919, fractionating cæsium alum and cæsium perchlorate obtained from the mineral pollucite. In all cases spectrum analysis of the final products of fractionation failed to yield any lines that could not be attributed to elements already known. These final products were also examined for signs of radioactivity, with negative results. Likewise in further studies of radioactive decomposition no

evidence has been found for an element having the properties of an alkaline metal.

No work reported has been done in an attempt to isolate element 85, which when discovered will be in the same group with iodine.

The following list indicates other elements of recent discovery:

Number	*Name*	*Discoverer*	*Country*	*Year*
72	Hafnium	Coster and Hevesy	Denmark	1923
43	Masurium	Noddack	Germany	1925
75	Rhenium	Heyrovsky and		
	Bohemium	Doleysek	Czecho-Slovakia	1925
61	Illinium	Hopkins	United States	1926
87	Ekacæsium	Undiscovered		
85	Unknown halogen	Undiscovered		

There are places for ninety-two chemical elements in the scheme of things as now conceived by the chemists. All but 87 and 85 have been filled. But some believe that there is a possibility that there may exist elements 93, 94, and 95, heavier than uranium, which is 92. Discovery of 75 is disputed.—*Science Service.*

Coal Dust Explosions.—The use of powdered coal is increasing. The hazards involved in it having proved serious, have been extensively investigated by the U. S. Bureau of Mines. In a recently issued Bulletin (242), of that bureau a summary is given of both experiments, observations and investigations of accidents. It has long been recognized that combustible dusts of all types are capable of causing violent explosions, even aluminum dust having this property. The Bureau of Mines discovered some years ago that starch dust in admixture with air is a most powerful explosive.

Powdered coal offers considerable advantage as fuel. It has been found especially applicable in plants that have been originally established to operate with natural gas, when the supply of this has declined, since the furnaces are not adapted to the usual form of coal. The application of powdered coal is useful when a very high temperature is required. As the supply of natural gas may be expected to decline, the use of powdered fuel may be expected to increase and the fire and explosion hazards will become more and more important. The average fineness is such that 93 per cent. will pass through a hundred mesh screen and 71 per cent. through one of 200 mesh. Coal which is retained on a twenty-mesh screen is not a cause of explosion.

Of course, the coal even of the most extreme fineness is not explosive in bulk, but only when thoroughly mixed with air. On the other hand such coal is liable to spontaneous combustion. The liability to explosion will depend not merely on the fineness of the grains but upon the percentage of inert matter. The amount of incombustible matter in the material that will render it non-explosive is directly proportional to the ratio of the volatile matter to the total combustible, and is expressed by dividing the per cent. of volatile matter by the same datum plus the fixed carbon, but the rule will not apply to a sample in which the ash of composition plus the inert matter equals 90 per cent.

The hazards in the use of powdered fuel are by no means limited to the use in furnaces. Accumulations of unused material in bins and on ledges of buildings, dust arising in the loading, unloading and other transfer of the fuel, set up dangerous conditions and many instances of serious accidents from such causes are detailed in the report. Even coal not specially powdered, such as "run-of-mine" or screenings, may cause disaster. In a Pittsburgh plant a short circuit formed by the accumulation of moist coal dust around the terminals of a back-connected electric switch caused the blowing out of the main fuse of installation with such violence that the fuse cartridges were shattered and the main panel partly wrecked. Fortunately the accident occurred at a time when the works were shut down and no dust particles were distributed in the air. Open lights in dusty places are a common source of accidents. It must be borne in mind that an unbroken electric light bulb may cause trouble if it is covered with dust. A workman, cleaning a bin, might leave a lamp burning that in time would be covered by the powdered fuel filled into the bin. This lamp would bring about spontaneous combustion.

In the summary of the data given in the report, emphasis is properly laid upon the importance of workmen using care and attention in all operations about the plant. The most perfect installation cannot make it fully "fool-proof." It is especially important that all persons employed about a plant using pulverized coal should be fully aware of explosiveness of any combustible dust mixed with air. The danger is greater because the accumulation of dust in corners and on ledges is not likely to attract attention. A leak of gas is usually soon noticed but powdered fuel is inoderous. Many rules for operation of plants using powdered fuel are given in the report, which is well worth the attention of all persons interested. H. L.

ICE CREAM.—The University of New Hampshire has recently published a bulletin on this topic, prepared by H. F. DePew and S. W. Dyer. The first manufacture of it is not known, but it seems to have originated in Italy and passed to France in the sixteenth century. From France it, of course, entered England, and then the United States. The last named country has developed its use to a far greater extent than any other. It is, indeed, the national dessert. It appears to have been first made in this country in 1851 by Jacob Fussell, a milk dealer in Baltimore, whose method was crude and the output only a few quarts a day. At the present time the output of American factories is about 300,000,000 gallons per day. It is still within the memory of many persons when ice cream and soft drinks were consumed only in the summer season, but they are now all-the-year-round refreshments.

The bulletin gives many interesting and important data concerning the composition of standard creams. Inasmuch as it is usually sold by volume, either in definite measures or in the cones, small and large, the manufacturers regularly increase the bulk by the introduction of air. This is termed "overrun." An example is given to show the method of calculation for this adulteration, from which it seems that 80 per cent. of air admixture is common. A gallon of the "mix", which is the completed product prior to air introduction, is given as weighing nine pounds, and after aeration the same volume may weigh only five pounds. Probably most ice cream eaters would prefer to have the article "flat," but it seems this is not possible for the general market article. Standard creams usually contain from 34 to 40 per cent. of solids of excellent digestibility and good food value. Comparisons by Benedict of the calories of ice cream with some other standard foods show that the former compares very favorably. It contains both A and B vitamins and a fair amount of mineral matter.

Economic questions come, of course, into play in the manufacture of ice cream for the market. Substances are used to replace the standard ingredients, to save expense. Thus, cane sugar is replaced by glucose from starch. Strong efforts are now being made to obtain the right to market starch sugar under names which do not suggest its source. As this sugar has less sweetening power than cane sugar, a larger amount can be used without oversweetening the mixture, hence a greater bulk of cream at less expense. Cornstarch has been used as an adulterant, but appears from the report not to be employed in the preparation of material on the large scale. It was formerly

included in recipes for domestic preparation. Several substances are used as "stabilizers," also called "binders" or "fillers," to increase the firmness of the article, help it to resist melting, and bind the several solid ingredients. Gelatin is mostly used. It should be, of course, of very good quality. Agar is not mentioned in the report, but a dealer in drugs who had a large trade in food and beverage materials stated that agar was used largely in the material sold in summer under the name "hokey-pokey." Obviously it was used because its jelly will stand up under a temperature decidedly higher than that of gelatin.

The report deals rather leniently with the several substitutes for the standard materials of ice cream, which should be cream, cane sugar, milk solids—not fat—and real flavoring. It seems, however, that the diner at restaurants and partaker of banquets will have to be content to get a certain amount of glucose, gelatin and air with his dessert.

HENRY LEFFMANN.

LECTURE ROOMS AND LABORATORIES ACCORDING TO MODERN METHODS.—In the past twenty-five years or so great changes have occurred in the facilities for instruction in science. The introduction of commercial service of electricity has caused great improvement in the methods of lighting and has enabled the employment of simple apparatus for power and especially for lantern projection. The combined reflecting and projecting lantern, with high-power incandescent lamps, makes illustration on the screen very easy. The work of illumination engineers has put into common use systems of illumination of the lecture room that leave little to be desired as far as efficiency and convenience are concerned. Studies of ventilation have greatly changed our views as to the real question in the ventilation of halls. It is now established that the principal problem is to get rid of excess of moisture and to bring about a circulation of the air. Deficiency of oxygen and excess of carbon dioxide are not the usual causes of the uncomfortableness of crowded auditoriums.

In view of these changes in both theory and practice, it behooves those who are constructing halls for scientific lectures to make material changes in plan both for lighting and ventilation. It will be worth while to set forth some of the points that should be observed. Auditoriums should be on the ground floor and should have one or more emergency exits, depending on seating capacity. No windows are needed. Windows do not afford either proper light or proper ven-

tilation. If they are back of the lecturer they annoy the audience. If in front, they annoy the lecturer. If on either or both sides, they annoy both parties. They are useless for ventilating purposes. In cold weather they cannot be opened without greatly annoying those near to them. On account of the cooling power of glass, a large window even when closed interferes seriously with the heating. In the warmer season, open windows admit dust and noise. In the now almost universal use of the lantern in scientific lectures, educational or popular, windows interfere seriously, for they have to be darkened, and even the best methods for this purpose give but partial concealment. The excellent methods of illumination now available render the window unnecessary. By having the hall lighted only by electric methods, a dark room can be obtained in a second and light can be restored equally promptly. This permits the lecturer to use slides interruptedly as occasion arises. It has the advantage that the major portion of the lecture when strictly educational can be given in full light so that students can take notes and be shown illustrative experiments.

Ventilation of lecture rooms must be by means of fans. The air should be taken out, passed through an apparatus to reduce its moisture and filter it, but not thoroughly dry it, and returned to the hall. In this way comparatively little heat will be lost and a saving in fuel secured, which in the present days of high and continually increasing cost of fuel is no minor matter. After the hall is emptied, the fan can be used to draw out the air so as to renew the supply by air admitted from outside. This air should be filtered. All lecture rooms should be provided with a powerful vacuum cleaning apparatus.

Many types of laboratories are now needed in educational work, but some of these, such as those in which the microscope is used, may do very well with artificial light. The chemical laboratory requires daylight, and not only good, regular ventilation, but emergency ventilation on account of occasional accident. It should be placed in the highest story and have a saw-tooth roof such as is now much used in mills, with the glass part fronting north. This location will give quiet, freedom from dust, and good lighting. Much expense for artificial illumination will be saved. An incidental advantage in the high location is that fall-pumps may be used in the rapid filtration apparatus instead of pressure-pumps, by which economy of installation and operation is secured and also less noise and splashing. The balances should, of course, be carried on a support independent of the room at large, but

this is easily obtained. Facilities for artificial illumination should be installed to provide for dark days and occasional work after daylight hours, but, as a general rule, it will be found that the upper floor laboratory will require but little artificial light. Shelves at tables should be avoided as far as possible. All tables should be provided with electric attachment. It is not necessary that the ceiling be very lofty. A room should be provided for operations attended by evolution of corrosive or irritating gases. The ordinary practice for such purpose of having a hood in the main room is objectionable. H. L.

MEDICAL AND PHARMACEUTICAL NOTES

THE STUDY OF CANCER.—Two facts about the fundamental nature of malignant tumor, which may bring nearer the conquest of cancer in man, have been discovered by Mrs. Margaret R. Lewis, anatomist of the Carnegie Institution, and Howard B. Andervont, Johns Hopkins graduate student, conducting joint research at the Johns Hopkins University.

First, they found that, for one form in the chicken at least, cancer is a mass of white blood cells or corpuscles. White blood cells desert their normal function of being the soldiers of the body that repulse invading germs and poison, and, instead, run wild, multiply and gorge themselves until they form a mass of malignant tumor. Heretofore the nature and exact origin of the cancerous mass has been unknown.

Second, the investigators have discovered that cancer can be transmitted simply by injecting into the muscles of a well chicken either the blood plasma or the white blood cells of a chicken suffering from cancer. Not only is the simple inoculation by transplanted blood successful, but serial inoculations by means of blood have been continued through as many as four generations of malignant tumors. This is evidence of the infectious nature of cancer, for, while heretofore it has been demonstrated that portions of cancerous tissue when transplanted will produce cancer in another animal, it was not known that one could thus transmit the infectious virus repeatedly from animal to animal by means of either the blood plasma or the white blood cells. A statement by Dr. Lewis follows:

The cancer cell is a blood cell. To be sure, it is a greatly changed white blood cell, but nevertheless quite comparable with the white blood cell which grows in tissue cultures. This cell is not characterized so much by the fact that it ingests and digests foreign material as it does at any site of inflammation, as it is by the fact that in this particular case it becomes abnormally enlarged and multiplies greatly at the site of the tumor. The cells increase to such an extent and digest away the surrounding tissue that they invade the muscle of the chicken and are carried to other organs where they bring about the death of the host.

The cells in their over-stimulated condition produce an active agent and this agent is present in the blood stream of the tumor chicken as well as in the white blood cells themselves. For when the white blood cells are separated from the blood fluid leaving only the clear plasma, this plasma upon inoculation into the muscle of a chicken produces a cancer by setting up an irritation in the inoculated region which draws the white blood cells to this region, and these cells become stimulated to abnormal activity by the tumor-producing substance in the plasma.

It is a fact well known to all surgeons that inflammation itself results in some growth-promoting substance which effects repair of the injured tissue and in some instances results in a greater increase of tissue than was lost. Dr. Alexis Carrel showed that the white blood cells themselves contain a growth-promoting factor. In any inflammatory reaction, regardless of how it is brought about, the white blood cells accumulate in great numbers in the region injured and there take up and digest or remove the irritating factor. This cannot yet be shown to be the cause of cancer, but we have shown that in the chicken at least it is the underlying factor concerned in the production of the cancer. Just what it is that causes the cells to go further and to enlarge more and multiply more until instead of repairing the injury they invade the tissue and bring about the death of the host is a matter we hope to know more about later.

Whether these results can yet be applied to higher animals or to human beings has not yet been determined. There is no question but that the human cancer is partly made up of blood cells and that it can in some instances be shown to be the result of slow inflammatory conditions. Whether the active principle is contained in the blood of human beings remains to be determined. At any rate the underlying factor concerned in all the tumors which have so far been produced by

bacteria, by virus, by chemicals or by parisites is a slow inflammatory reaction with the resulting accumulation of white blood cells in the injured region.—*Science Service.*

HEAT AND LIGHT ALLERGY.—The fairy story princess who spent a miserable night because of a pea concealed under the nine mattresses in her bed was no more sensitive than some everyday human beings.

In the laboratories of Dr. W. W. Duke, in this city, hay fever and asthma are being studied, and he has shown that an individual may be sensitive to light or to certain temperatures, just as hay fever victims are sensitive to ragweed pollen or other proteins.

Dr. Duke has illustrated with human patients how weals can be produced in a very few moments on the body of a person who is sensitive to heat or cold or light, and he has shown how such exposure to a physical agent may lead to asthma or to all the symptoms of anaphylactic shock.

Persons are sometimes sensitive, Dr. Duke finds, not to many degrees of cold but only to a definite small range of temperature, as from ten to fourteen degrees above freezing. These patients showed no sensitivity to a temperature around the freezing point. Ice could be pressed against their skin without producing abnormal effects. Yet a short exposure of an area of the skin to a slightly higher temperature produced ugly weals.

This type of case has been little studied and is almost unknown to the average physician. No cure is known for it. The person who is sensitive to a protein can be treated with gradually increasing doses of the toxic substance until his tolerance is much greater, but the patient who is supersensitive to light or heat must always avoid the particular type of radiation that poisons him.

The condition, which is known to medical science as allergy, may be produced not only by pollen proteins and radiations, but also by smokes, meat and fish proteins, and fish glue. There are a number of theories as to the cause of allergy, Dr. Duke explains, but so far none has been substantiated.—*Science Service.*

A MEDICAL PRESCRIPTION NOT A PRIVATE DOCUMENT.—A pharmaceutic chemist residing in Szombathely, Hungary, has impeached a local estate owner for having forged the name of a physician on a

prescription in order to obtain morphine. The chemist had furnished the drug several times, but finally discovered that the signature of the physician was forged. He duly reported the case, and the public prosecutor charged the estate owner with having forged a private document. The indicted wrote on the prescription the words: "Repetatur semper Dr. Szatmári." The counsel for the defense tried to prove that a prescription is not a public document, but a simple form of order. The Court thereupon dropped the accusation of forging a private document, but maintained the charge of an offense against public safety and getting a poison by false pretenses and fined the estate owner 1,000,000 crowns ($15) and costs.—*Journ. Am. Med. Assoc.*

More Bootleg Cosmetics.—The February issue of *Health,* the official bulletin of the New Hampshire State Board of Health, contains information concerning the sale of arsenical "hair tonics," which are especially advertised for the cure of dandruff and scalp eczemas. The chemist of the board, Mr. Charles D. Howard, has made analyses of a number of these preparations. Injurious effects have been noted as resulting from several of these. In one case it is stated that the maker of the tonic sought to settle the case by a money payment, but in most cases the labels are so worded as to avoid any responsibility. One label, for instance, states: "Physicians maintain that the idiosyncrasy of some people subjects them to ill effects when using certain foods and remedies beneficial to mankind; therefore in such cases we disclaim responsibility." H. L.

A New MS. of Dioscorides.—French pharmacists have a society devoted to collecting and publishing data concerning the history of pharmacy. It was founded in 1913, has now a large membership and publishes a bulletin. The issue for January, 1926, contains a very appreciative review of the first two volumes of *Popular Science Talks.* At the meeting of December 19, 1925, Mr. Mazloum gave a brief account of a MS. of Dioscorides. There is some ambiguity in the announcement, since it is stated to be a "recent discovery," yet it is further stated that it was found at Venice in the seventeenth century, was at Constantinople about 1850, then went to Rumania, where it was purchased by an American collector, who brought it to Paris a

few years ago. It is promised that it will soon be reproduced by photography. It contains about 300 leaves, and dates from about the eleventh century. The text is in Greek, but the numerous figures of plants are designated by Arabic names. H. L.

"APPROVED" SCARLET FEVER PRODUCTS ARE SO LABELED.—The large incidence of scarlet fever cases in recent months has greatly stimulated interest in scarlet fever antitoxin, several authorities having announced, within the past few years, methods for the preparation of an antitoxin for this disease.

The work of Dr. G. F. Dick and Dr. G. H. Dick, of Chicago, in the development of a toxin from the scarlet fever streptococcus, and then of an antitoxin, is probably the best known contribution in this direction. In order to safeguard the character and quality of the products which might be prepared after their method, the Dicks applied for and received patents from the United States Government, and these patents are now being administered by the Scarlet Fever Committee.

Physicians desiring to use scarlet fever antitoxin prepared after the Dick method are therefore enabled to make quite certain that they are getting the correct product as ordered, because every package of scarlet fever antitoxin that is approved or authorized by the Scarlet Fever Committee bears a notation to that effect.

The same notation likewise protects the druggist, who might otherwise be in doubt as to whether the product he is handling had been made after the Dick method or after some other method. The note of approval by the Scarlet Fever Committee is your protection.

The Mulford Biological Laboratories are supplying a scarlet fever antitoxin (Dick method) that is approved not only by the Scarlet Fever Committee but also by the United States Hygienic Laboratory, so that, in addition to the well-known Mulford reputation for quality, their product carries also these other two authoritative approvals.

There is a therapeutic package and a prophylactic package, each dose being put up in a convenient and ready-to-use syringe container.

Further information and literature regarding this most timely item may be obtained by writing to H. K. Mulford Company, Mulford Building, Philadelphia, Pa., and mentioning this publication.

NEWS ITEMS AND PERSONAL NOTES

NEW OFFICERS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION (1926-1927).—Theodore J. Bradley, dean of the Massachusetts College of Pharmacy, Boston, has been elected president of the American Pharmaceutical Association for 1926-1927. Dean Bradley was chosen by a national ballot of the entire membership of the association.

George Judisch, of Ames, Iowa, was named first vice-president. He is a member of the Iowa State Board of Pharmacy. Arthur G. Hulett, of Phoenix, Ariz., a member of the Board of Pharmacy of that State, was elected vice-president.

Members of the association's council for next year are: Dr. James H. Beal, Urbana, Ill.; Charles H. LaWall, dean of the Philadelphia College of Pharmacy and Science; William B. Day, of Chicago, dean of the College of Pharmacy in the University of Illinois.

NATIONAL FORMULARY BECOMES OFFICIAL JULY 1, 1926.—The Council of the American Pharmaceutical Association has decided that the *National Formulary V* shall become official July 1. The edition will be ready for distribution during the early part of April, probably before the 15th. The general distributors are the Chemical Catalog Company, 19 East Twenty-fourth Street, New York City, to whom all orders for the *National Formulary V* should be addressed. Several subagencies will be appointed and their names can be obtained by addressing the Chemical Catalog Company.

AMERICAN PHARMACEUTICAL ASSOCIATION COMMITTEE ON RESEARCH.—The American Pharmaceutical Association has available a sum amounting to $450 which will be expended after October 1, 1926, for the encouragement of research.

Investigators desiring financial aid in their work will communicate before June 1 with H. V. Arny, chairman A. Ph. A. Research Committee, 115 West Sixty-eighth Street, New York, N. Y., giving their past record and outlining the particular line of work for which the grant is desired.

PROFESSOR COOK ADDRESSES NEW JERSEY COLLEGE OF PHARMACY STUDENTS.—Prof. E. Fullerton Cook, of the Philadelphia College of Pharmacy, chairman of the Committee of Revision of the United States Pharmacopœia, was the principal speaker at the annual banquet and ball of the students of the New Jersey College of Pharmacy, which was held at the Washington Restaurant, Newark, March 10. Professor Cook spoke of the nature of the work of the pharmacist and said that both the professional side of service to humanity and the commercial side must be studied and carried on in the truly ethical spirit if the pharmacist is to give to the community the full measure of service. He spoke of the hearty and cordial acceptance of the tenth edition of the *Pharmacopœia* that has just been issued by the three groups most concerned, namely, the physicians, the pharmacist, and the government officials concerned with the enforcement of the food and drug laws.

Prof. Ernest Little acted as toastmaster, introducing the other speakers as follows: Dr. Caswell A. Mayo, dean; Dr. P. E. Hommel, dean emeritus; and Prof. A. Marquier of the New Jersey College of Pharmacy; H. W. Crookes, former president of the New Jersey Board of Pharmacy, and R. E. Parks and Rubin Poleshuck, presidents of the senior and freshman classes, respectively.

FOUNDER'S DAY CELEBRATION.—Founder's Day at the Philadelphia College of Pharmacy and Science was appropriately celebrated on Tuesday, February 23. An afternoon program was given in the auditorium of the college, in which short addresses were made by Dr. Braisted and Professors LaWall and Sturmer, and musical selections and recitations were given by home talent.

In the evening a drug store play was given at the auditorium of the central branch of the Y. M. C. A. The members of the cast were junior faculty members and students. A large audience enjoyed every minute of the performance. This is the same play that was presented at the 1925 meeting of the Pennsylvania Pharmaceutical Association in Washington, Pa., last June with such success.

PROFESSOR JOSEPH G. NOH BECOMES FULL TIME SECRETARY OF THE PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.—With the view of rendering constructive service to its members, the Pennsyl-

vania Pharmaceutical Association have secured the services of Joseph G. Noh of Purdue University, for their full time secretary, with permanent offices in Harrisburg. The secretary will assist in the organization of county or local associations, maintain the employment service for members, protect the interest of the pharmacist in legislative matters, maintain a complete file of State and Federal Narcotic, Prohibition and Pharmacy laws, and edit a monthly letter or bulletin to the members.

George F. Lee, of Johnstown, Pa., president of the association, feels the association was fortunate in securing the services of Mr. Noh who was born and reared in Clarkson, Nebraska. After receiving his early education in the schools of Clarkson he entered the University of Nebraska and received the degree of Graduate in Pharmacy. He continued his studies at the same university graduating with highest honors and receiving the degree of Pharmaceutical Chemist followed by the degree of Bachelor of Science in Pharmacy.

After serving as an assistant instructor in the pharmacy department of the university for two years, Professor Noh accepted the position of assistant professor of pharmacognosy and botany at the New Jersey College of Pharmacy. In 1924 he was advanced to the position of associate professor and department head. While with the New Jersey College Professor Noh served as a member of the Publication Board, chairman of the board of athletic directors, class advisor and secretary of the faculty.

At the present time newly appointed secretary is on the faculty of Purdue University, teaching general pharmacy, prescription compounding, and commercial pharmacy. He is a member of Phi Delta Theta, Kappa Psi, and Scabbard and Blade Fraternities, the American Pharmaceutical Association, New Jersey Pharmaceutical Association and the American Chemical Society.

STATUE OF DR. CRAWFORD W. LONG—DISCOVERER OF ETHER ANESTHESIA IN HALL OF FAME.—Dr. Joseph Jacobs, pioneer Atlanta pharmacist, and a graduate of the Philadelphia College of Pharmacy —friend and former employee of Crawford W. Long, discoverer of ether anesthesia—has been largely instrumental in keeping fresh the memory of one of mankind's greatest benefactors. It was through the interest and enthusiasm of Dr. Jacobs and many other well known

Georgia doctors and pharmacists that Dr. Long's statue has been recently placed in the Hall of Fame in Washington.

The unveiling ceremony occurred March 30th, in Statuary Hall, National Capitol, Washington, D. C., the eighty seventh anniversary of ether anesthesia discovery. Dr. Jacobs was the first speaker at the dedicatory exercises.

PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE NEWS NOTES

The P. C. P. and S. Boys' basketball team has just finished a successful season, having played City College League and outside games.

The P. C. P. and S. Girls' basketball team had a late start, played but two games, losing one to Osteopathy and winning one from West Philadelphia Y. W. C. A. This is the first year for the girl's team and we have high hopes for next year, as most of the girls will be here again next season.

The track team competed in the City College meet at the Y. M. C. A., March 25th, and will compete in the City College Penn Relay April 27th, and possibly other dual meets.

A baseball team organized this year, the first for about ten years. They do not expect to do very much this year, but will get well organized in order to do some good work next year.

Honorable Franklin Spencer Edmonds, of Philadelphia, addressed the senior student assembly at one of its meetings in Philadelphia, and gave the boys a splendid talk on the responsibilities of citizenship which was very much appreciated.

The classes in botany and biology of the college were taken to the recent flower show held in the Commercial Museum in West Philadelphia, in small groups, by the professors and instructors in the department.

The class in advanced operative pharmacy, numbering about thirty, visited the manufacturing plant of Johnson and Johnson and the biological and ether plant of E. R. Squibbs & Co., in New Brunswick, N. J., during February, an entire day being devoted to the

combined trip. Professors LaWall and Nichols went with one group and Professors Cook and Griffith with the other, as small groups only are taken through Johnson and Johnson's laboratories.

The class in advanced operative pharmacy visited the biological and manufacturing laboratories of H. K. Mulford Co., during February under the guidance of Professor E. Fullerton Cook.

The entire Ph.G. graduating class will visit the manufacturing laboratory of Smith, Kline and French Co. during April. Several sections will be accompanied separately in the time ordinarily devoted to the period of laboratory work.

Dr. Edward Spease, Dean of the Department of Pharmacy, Western Reserve University, made a short visit to the college during March, was entertained at luncheon by several members of the faculty and at dinner in the evening by the members of the Epsilon Chapter of Phi Delta Chi Fraternity of which Dr. Spease is now the national president.

The graduating class has elected a fund sufficiently large to present to the college a synchronized clock which will also sound the end of the period.

Dr. Charles H. LaWall, Dean, delivered a lecture on Pure Foods to the St. Davids Society recently in Philadelphia, and also a lecture on the Romance of Medicines before the northern branch of the Philadelphia County Medical Society.

Prof. E. Fullerton Cook recently addressed the Atlantic County Drug Club at a meeting held in Atlantic City, N. J.

Professors Charles H. LaWall, E. Fullerton Cook, and Horatio C. Wood, Jr., attended a meeting of the Executive Committee of Revision of the U. S. Pharmacopœia in New York on Saturday, April 3d, to discuss research plans in connection with the next revision of the Pharmacopœia.

Dr. Tsungming Tu, professor of pharmacology, Medical College, and chief of the pharmacological laboratory, Government Research Institute of Formosa, was a recent visitor at the college.

Plans are under way to give a testimonial dinner to the members of the cast and the student orchestras who contributed to the success of Founders' Day exercises.

BOOK REVIEWS

THE EXTRA PHARMACOPŒIA OF MARTINDALE AND WESTCOTT. Revised by W. Harrison Martindale, Ph. D., Ph. Ch., F. C. S., and W. Wynn Westcott, M. B. London, D. P. H. 18th Edition, Vol. II, 728 pp.; 20s. The Complete Work in 2 Vol.; 47s 6d. H. K. Lewis & Co., Ltd., 136 Gower St., London, W. C. I.

The referee had the pleasure to review volume I of "The Extra Pharmacopœia" in AMERICAN JOURNAL OF PHARMACY, March, 1925, pp. 203 to 205, which review brought forth a number of inquiries, showing that this excellent work is becoming better known on this side of the Atlantic, an advantage which "Martindale" fully deserves. The broad separating lines of the two volumes may be said to be the following: Volume I contains matters pertaining to treatment and is to be kept of such size as to be conveniently carried in the pocket of physician and pharmacist; volume II contains that portion of the work dealing chiefly with analytical, experimental and research data.

The list of abbreviations contains five closely printed pages and includes U. S. P., N. F., U. S. D., not forgetting A. J. PH. The Analytical Addenda to Materia Medica in volume I occupy 160 pages in volume II. Among the other analytical data I beg to point out the following important ones: Indicators, Determination of Hydrogen Ion Concentration of Solutions, Different Tables, Analysis of Urine, Blood, Fæces, Stomach Contents, Water, Milk, Butter, etc.

The following chapters of practical use to pharmacist, physician and chemist may be mentioned: Freezing Mixtures, Drop Table, Physiological Action and Chemical Constitution, Sterilization, Antiseptic Powers of Chemicals and Disinfectants and Removal of Stains on Cloth and the Skin. An Analysis of 15,000 British Prescriptions gives the frequency of the ordered medicaments in the following rotation: Spirit of Chloroform, Sodium Bicarbonate and Tincture of Nux Vomica. A glossary of nine closely printed pages gives the English translation of terms used in Arabic, Belgian, Danish, Dutch, French, German, Italian, Portuguese and Spanish prescriptions. This alone is worth the price of the two volumes to the pharmacist who dispenses foreign prescriptions.

For the practicing pharmacist, physician and chemist, volume II is equally as important as volume I. We wish the eighteenth edition of "Martindale" the best of success and a long life!

THE CHEMISTS' DICTIONARY OF MEDICAL TERMS. 4th Edition. 283 pp. The Chemist & Druggist, 42 Cannon Street, London, E. C. 4. Price, $1.00.

The basis of this Dictionary was a treatise which was published in *The Chemists' and Druggists' Diary for 1907*. It was written by a general medical practitioner, who is also an experienced pharmacist, and, consequently, was in a position to judge what is desired and required by retail chemists, for whom this Dictionary is intended. During the nine years which have elapsed since the previous edition, many changes have occurred in medical and surgical nomenclature. These new terms and definitions have been incorporated in the present fourth edition.

Several anatomical diagrams are included at the end of the book, namely: The Organs of the Body, the Alimentary Canal, and two views of the Human Skeleton.

This "Chemists' Dictionary of Medical Terms" should be in the hands of every pharmacist also in the United States.

OTTO RAUBENHEIMER, PH. M.

HANDBUCH DER PRAKTISCHER UND WISSENSCHAFTLICHEN PHARMAZIE. Unter Mitarbeit erster Fachgenossen herausgegeben von Geh. Reg.-Rat Prof. Dr. Hermann Thoms, Director des pharm. Instituts der Universitat in Berlin. 6 Lexicon Volumes. Urban & Schwarzenberg, Berlin and Wien.

This classic work is now more than half completed. Volumes I and II were reviewed in AMERICAN JOURNAL OF PHARMACY, October, 1924; pp. 791 and 792. Volume I treats of Commercial Pharmacy, Wholesale, Manufacturing, Retail and Dispensing Pharmacy. Volume II contains a description of the physical, chemical and biological methods and assays and the manufacture, properties and tests of plant products.

Volume III, just completed and before us, is divided into two parts. A. Foods and Beverages, Their Description, Manufacture and Analysis. Among the thirty chapters, each prepared by an expert in that respective field, I beg to point out the following: Mineral Waters and Salts, by E. Hintz and L. Fresenius in Wiesbaden, pp. 89-109; Carbohydrates (Sugars, Starches, Bread, Cake and Infant Foods),

by O. Keller in Jena, pp. 126-185; Meat, Beef Extracts, Peptone, etc., by E. Spath in Erlangen, pp. 337-412; Lecithin, by Erich Reinger in Berlin, pp. 424-428; Milk, by P. Borinski in Berlin, pp. 458-485; Beverages Containing Alkaloids (Coffee, Tea and Cacao), by O. Keller in Jena, pp. 609-653; Tobacco, by R. Kissling in Bremen, pp. 721-736. In these "dry" times, I almost forgot to mention the excellent chapter on Beer, Wine and Liquors, the mere reading of which "makes the mouth water."

B. Technical Products, Their Description, Manufacture and Analysis. Among the many excellent chapters I want to mention the following headings: Soaps, by W. Schrauth in Rodleben; Detergents and Cleaning Fluids, by L. Kroeber in München; Glass, Ceramics and Cement, by H. Hecht in Berlin; Paper by G. Schwalbe, Eberswalde; Glue, Gums and Gelatine, by M. Bottler in Würzburg; Mineral Oils, by R. Kissling in Bremen; Inks, by H. v. Haasy in Dresden; Alloys, by E. H. Schulz in Dortmund, and Fibers, Cotton, etc., by Dr. A. Voight in Hamburg. Perhaps needless to state that the work is full of historical data, which are quite an advantage. At the end of each chapter we find a complete bibliography, a great help to student, pharmacist and teacher. The literature of the entire world has been consulted and, needless to say, the United States has not been forgotten.

The volume before us comprises 1320 pages and verily is a master work, and above all a practical handbook. The entire work, in six volumes, is a monumental classic work, a credit to Prof. Dr. Hermann Thoms and his collaborators and also to the publishers. Pharmacy—professional pharmacy—can be justly proud of this "Handbook of Practical and Scientific Pharmacy." Let us hope that the work will also become well known in the United States.

Otto Raubenheimer, Ph. M.